ENVIRONMENTAL TOBACCO SMOKE:

A REVIEW OF THE LITERATURE

August, 1991

2023468932

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

TABLE OF CONTENTS

I. INTRODUCTION 1

II. ENVIRONMENTAL TOBACCO SMOKE AND HEALTH CLAIMS 7
An Overview 7
Lung Cancer 12
Meta-Analysis of ETS Studies 23
Bias and Confounding Factors 26
Mathematical Models 32
Summary 35
Overall Mortality and Cancer Other Than the Lung 36
Lung Function/Disease 56
Adults 56
"Compromised Individuals" 66
Children 70
"Compromised Individuals" 87
Heart Disease 91
Experimental/Biochemical Studies 97
Other Children's Diseases and Conditions/Pregnancy . . . 105
Allergy 109
Sick Building Syndrome 114
Summary 117

III. ENVIRONMENTAL TOBACCO SMOKE AND INDOOR AIR QUALITY . . . 121
Sidestream Smoke 121
Biological Markers 123
Toxicity (Sidestream Smoke) 124
Constituents of ETS 125
Exposure to ETS 126
Carbon Monoxide 127
Particulates 128
Particulates and Radon 130
Nicotine 130
Other Constituents 133
Cotinine as a Marker for ETS Exposures 135
Other Determinations of ETS Exposure/Thresholds . 136
Summary 138

IV. ENVIRONMENTAL TOBACCO SMOKE AND THE PUBLIC 150
Governmental Regulations and Individual Rights 150
Governmental Reports 154
Court Decisions 157
Summary 162
Conclusion 163

2023468933

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

I. INTRODUCTION

The claim that exposure to environmental tobacco smoke (ETS) causes disease in nonsmokers has generated a great deal of public concern. Although a review of the scientific literature indicates that this claim has not been proved, it is used by anti-smokers in their efforts to make smoking socially unacceptable and, thereby, to create a "smoke-free" society. The importance of the ETS/health issue to the antismoking movement is demonstrated by the comment of the then director of the U.S. Office of Smoking and Health that "of all the issues, this [ETS] is the one that will propel the United States toward a smoke-free society."[1]

The campaign for a "smoke-free" society has been characterized by one sociologist as follows:

> The strategy, quite overtly, is to progressively stigmatize smoking, segregating the smoker in all public places, and eventually to eliminate smoking as a socially acceptable custom. How is this to be made politically palatable? The answer is clear: by suggesting that smoking harms not only the smoker, but various categories of "innocent bystanders."[2]

The questionable and often contradictory nature of studies concerning ETS exposure and disease is largely ignored by the anti-smoker; the goal is to achieve publicity and arouse emotion.

2023468934

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In addition, the issue of nonsmoker exposure to ETS has become the means by which antismokers seek to enact legislation regulating smoking in the workplace and other public places. Here again, the strategy of using the ETS/health argument to modify smoking behavior is apparent. For example, the chairperson of the U.S. National Academy of Sciences committee which authored a 1986 report on ETS remarked that "legislation could also be justified, not because it will have much effect on the occurrence of lung cancer among nonsmokers, but because it may motivate some people either to stop smoking or never to start."[3] In 1990, antismoking activists depicted the ETS issue as a "Trojan horse" because, they contended, smokers will benefit "from the significant reductions in smoking frequency that occur with the proliferation of smoking restrictions introduced in the name of concern for the health of nonsmokers."[4]

Indeed, one reviewer has observed that there are even instances in the scientific literature in which calls are made to establish ETS as harmful "as a means to limit smoking."[5] Scientists with personal motivations against smoking now publicly declare that the "lack of definite scientific evidence" [regarding ETS] should not obstruct efforts in "encouraging adults to give up smoking,"[6] and that "the totality of evidence [on ETS and disease in nonsmokers] is sufficient for public health purposes."[7]

2023468935

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

A German professor of social medicine, Dr. J. von Troschke, recently discussed the tendency of some scientists and physicians to "dramatize the discussion about passive smoking."[8] Dr. von Troschke suggested that such behavior may be an attempt "to compensate for the frustrations" encountered in convincing smokers to quit. He observed that "it is natural to convert one's own frustrations into aggression against the resisting smokers and gladly employ every means by which one can bring pressure to bear." One of those means, Dr. von Troschke said, is "the argument on damaging the 'innocent nonsmokers' health.'"

Similarly, Dr. Gio Gori of the Health Policy Center in the U.S. commented:

> The whole ETS question has been raised as a tool in the larger battle against smoking, and therefore, it has been used with the principle that the end justifies the means, and I think as a scientist myself that many people . . . would be rather taken aback by this misuse of science. . . [T]here are many other examples in our society today where science is misused for political reasons, in regulation as well as in establishing public health policy. The justification of course, is usually that we have to take action on the basis of imperfect knowledge for prudent reasons, but I think that many in our society question how far can we go with prudence because prudence itself could become very dangerous beyond a certain point.[9]

2023468936

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

The tactic of using the ETS/health argument to modify smoking behavior also has been criticized in the international press. One columnist for The (London) Times noted that while she agreed in principle with the antismoking movement, she could not condone "the lying that accompanies it." She explained: "The lie is the claim that the health hazards of second-hand smoke have been scientifically established."[10] Similarly, a writer for a German publication called the use of the ETS/health argument an "unethical" tactic intended to instill "anxiety in the nonsmoker" and "feelings of guilt in the smoker."[11]

Certainly, ignorance of scientific procedures and the inability or unwillingness to recognize faulty research methodology have contributed to the controversy on ETS. As one reviewer of the literature wrote in 1987:

> A pluralistic society such as ours has its lobbies. And it is they who have removed the subject of passive smoking from the scientific to the political stage. It would be wrong to impute this to bad intentions. Inadequate or biassed occupation with the problem, or general insecurity with regard to scientific comprehension, are quite enough.[12]

Given the importance of the ETS issue for the antismoking movement, the purpose of this paper is to review the current scientific literature regarding environmental tobacco smoke and disease in nonsmokers. It is intended to identify sources of

2023468937

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

information and misinformation about ETS in an effort to demonstrate that the weight of the available scientific evidence does not justify the claim that ETS causes disease in nonsmokers.

2023468938

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Introduction

1. Shopland, D., Quoted in "The Campaign Against Smoking Gains Momentum" by J.K. Iglehart, New Engl J Med 314(16): 1059-1064, April 17, 1986.

2. Berger, P., "A Sociological View of the Antismoking Phenomenon." In: Smoking and Society. R. Tollison (ed.). Lexington, Massachusetts, Lexington Books, D.C. Heath and Co., 225-240, 1986.

3. Hulka, B., Quoted in "Other People's Smoke May Be Risky for You" by S. Walton, National Research Council News Report 37(1): 8-11, December, 1986-January, 1987.

4. Chapman, S., et al., "Why the Tobacco Industry Fears the Passive Smoking Issue," Int J of Health Ser 20(3): 417-427, 1990.

5. Witorsch, P., "Passive Smoking," New Zealand Med J: 258-259, April 22, 1987.

6. Hugod, C., "Indoor Air Pollution from Tobacco Smoke as Seen by Scientists in Governmental Administration." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 390-392, 1990.

7. Samet, J., "Editorial Commentary: New Effects of Active and Passive Smoking on Reproduction?," Amer J of Epi 133(4): 348-350, 1991.

8. von Troschke, J., "The Public Discussion of Passive Smoking Is Being Conducted With Inappropriate Dramatics," Der Kassenarzt 35: 36-40, 1989. Translation.

9. Gori, G., "Panel Discussion and Overall Appraisal," The Toxicology Forum: 1990 European Meeting, Budapest, Hungary, 231-238, June 18-22, 1990.

10. Amiel, B., "Smoke in Their Eyes," The (London) Times: 15, March 13, 1987.

11. Kris, M., "High Risk of Cancer for Passive Smokers. More Than Much Ado About Nothing?," Aertze Zeiting 5(220): 2, December 11, 1986. Translation.

12. Adlkofer, F., "Probleme mit dem Passivrauchen (The Problems of Passive Smoking)," Der Kassenarzt 27(51/52): 29-39, 1987. Translation.

2023468939

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

II. ENVIRONMENTAL TOBACCO SMOKE AND HEALTH CLAIMS

An Overview

Antismokers typically refer to several highly publicized studies as "proof" that tobacco smoke is associated with disease in nonsmokers. The studies most frequently cited are those by Hirayama[1] and Trichopoulos, et al.,[2] who reported that nonsmokers married to smokers have a higher risk of developing lung cancer, and by White and Froeb,[3] who asserted that nonsmokers with long-term exposure to tobacco smoke in the workplace have significantly reduced small-airways function. Other reports have suggested that children and individuals with lung and heart disease are adversely affected by exposure to environmental tobacco smoke.

In addition, government health officials have issued reports which antismokers are using to pressure legislative bodies in the promotion of a "smoke-free" society. In 1986, two such reports in the U.S., one issued by a National Academy of Sciences committee to the U.S. Environmental Protection Agency (the NAS Report),[4] and the other by the Office of the Surgeon General,[5] concluded that ETS causes disease in nonsmokers. In 1988, the Independent Scientific Committee on Smoking and Health in the United Kingdom issued its report with conclusions similar to those of the U.S. Surgeon General.[6] Most recently, the U.S. Environmental

2023468940

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Protection Agency (EPA) issued for public review a draft risk assessment on ETS in which it recommended that ETS should be classified as a "known human carcinogen," that is, a cancer-causing substance.[7]

However, critical analyses of these studies and reports by physicians and scientists from around the world, together with other studies which report no association between ETS and human disease, indicate that such extreme health claims are highly suspect and not justified on a scientific basis. For example, in October, 1986, an international gathering of scientists in Essen, Germany, considered the experimental and toxicological findings regarding ETS.[8] Professor J.G. Gostomzyk, director of the Health Bureau in Augsburg, Germany, concluded in his review of the proceedings that "so far, even toxicology has not been able to ascertain with any greater degree of probability than did epidemiology that there exists a link between damage to health and passive smoking."[9]

In May of 1988, organizers of a symposium on ETS in Austria, entitled "Illness Due to Passive Smoking?," issued a press release in which they concluded that "a causal relationship between ETS and illness cannot be established" and that "there is no positive evidence that cancer and other such illnesses are caused by passive smoking."[10]

2023468941

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In his introduction to the published proceedings of a symposium on indoor air quality held in Argentina in 1988, Dr. Osvaldo Fustinoni, vice-president of the National Academy of Sciences in Buenos Aires, wrote that because of the uncertainty regarding scientific data on ETS exposures and health effects, "it is in question to what extent governments should establish regulations affecting individual freedom, legislating over private facilities like factories or cinemas, theatres, etc."[11]

In his "Summary and Concluding Remarks" from the proceedings of the 1989 International Symposium on ETS held at McGill University in Montreal, Canada, co-organizer Dr. Joseph Wu concluded that the published data on ETS, when critically examined and evaluated, do not provide a scientific justification for the claim that ETS is a cause of disease in nonsmokers.[12]

Dr. Hitoshi Kasuga, organizer of The International Conference on Indoor Air Quality in Tokyo, Japan, concluded in the proceedings published in 1990:

> Most participants were of the opinion that it would be very difficult at the present time to reasonably establish a correlation between passive smoking and lung cancer because a detailed examination of all published data (statistical bias in relationship between ETS and lung cancer, estimated ETS levels, incidence of lung cancer in nonsmokers, histological types, etc.) shows that the relationship, if one exists at all, is very slight.[13]

2023468942

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

ENVIRONMENTAL TOBACCO SMOKE AND HEALTH CLAIMS

An Overview

1. Hirayama, T., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer: A Study from Japan," British Medical Journal 282: 183-185, 1981.

2. Trichopoulos, D., Kalandidi, A., Sparros, L. and MacMahon, B., "Lung Cancer and Passive Smoking," International Journal of Cancer 27(1): 1-4, 1981.

3. White, J. and Froeb, H., "Small-Airways Dysfunction in Nonsmokers Chronically Exposed to Tobacco Smoke," New England Journal of Medicine 302(13): 720-723, 1980.

4. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

5. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

6. Department of Health and Social Security, Fourth Report of the Independent Scientific Committee on Smoking and Health. London, Her Majesty's Stationery Office, 1988.

7. U.S. Environmental Protection Agency, Office of Health and Environment Assessment, Office of Atmospheric and Indoor Air Programs, Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children. External Review Draft, EPA 600/6-90/006A, May, 1990.

8. Proceedings of the International Experimental Toxicology Symposium on Passive Smoking, Essen, Germany, October 23-25, 1986. E. Mohtashamipur (ed.). Published in Toxicology Letters 35(1): 1-168, 1987.

9. Gostomzyk, J., "Passive Smoking-Report on an International Symposium (23-25 October 1986)," Public Health 49: 212-215, 1987.

2023468943

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

10. Lehnert, G. and Wynder, E., "Illness Due to Passive Smoking?," Press Release, Vienna, Austria, May 3, 1988. Translation.

11. Fustinoni, O., "The Problem of Indoor Air Pollution: A Warning to Society." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 13-16, 1989.

12. Wu, J., "Summary and Concluding Remarks." In: Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989. D.J. Ecobichon and J.M. Wu (eds.). Lexington, Massachusetts, Lexington Books, D.C. Heath and Co., 367-375, 1990.

13. Kasuga, H., "Outline of the International Conference on Indoor Air Quality." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 509-510, 1990.

2023468944

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Lung Cancer

Although 29 studies on ETS and lung cancer with varying conclusions have been published to date, two highly publicized articles published in 1981 are still among the most frequently cited to support the claim that ETS exposure increases the nonsmoker's risk of lung cancer. A study of Japanese women by Dr. Takeshi Hirayama reported that nonsmoking wives of heavy smokers had a much greater risk of developing lung cancer than nonsmoking wives of nonsmokers.[1] In a study of Greek women, Trichopoulos, et al., concluded that a nonsmoking woman whose husband smoked had twice the risk of developing lung cancer as a nonsmoking woman married to a nonsmoker.[2]

Both studies have been widely criticized in the scientific literature. Numerous inadequacies and inconsistencies in the Hirayama study have been pointed out by noted scientists and physicians who have questioned the validity of its conclusions.[3-25] Dr. Ragnar Rylander, the organizer of the 1983 University of Geneva symposium on ETS, noted that the study had been criticized for its lack of questionnaire reliability, absence of histological or microscopic diagnosis, questionable statistical treatment, and failure to examine such factors as air pollution from heating and cooking.[24] A participant at the International Conference on Indoor Air Quality held in Tokyo in 1987 observed that Hirayama's study

2023468945

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

had been questioned for bias in statistical processing, as well as for failures to measure ETS exposure levels and to evaluate and report "dietary and occupational factors known to influence susceptibility to lung cancer."[6]

Moreover, several researchers have criticized Hirayama's techniques of age adjustment, an important consideration since age may act as a confounding or biasing factor in such calculations.[4-5,11-13] For instance, two studies presented at the Conference on Indoor and Ambient Air Quality, held at London's Imperial College in 1988, reported that Hirayama had not divided his study population into appropriate age groups.[4,11] Elsewhere, the authors of one of these studies noted that the risk Hirayama had reported for nonsmoking wives of smokers disappeared when such age bias was removed.[5] In a 1989 paper, another scientist also demonstrated the effect of age bias as well as a significant interaction between age and husband's smoking status in Hirayama's data.[25] At a conference held in Brussels in 1989, biostatistician Dr. S. James Kilpatrick reported that Hirayama would not have calculated a statistically significant elevated risk if he had used an appropriate statistical model and had adjusted his data by the wife's age rather than the husband's.[12] Hirayama has failed to address these and other issues raised by his critics, and, in fact, published a monograph in 1990 which again contains the criticized analyses and tables.[26]

2023468946

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Criticisms of the Trichopoulos, et al., study were acknowledged by the authors themselves in an update of their study, published two years after the original report.[27] In that update, they noted that their research had been "criticized (by ourselves and others) because of the small number of subjects, because several tumors lacked histological confirmation, and because controls and cases were from different hospitals." Two German scientists went so far as to describe the study as a "textbook example of how a case-control study should not be performed."[28] Nevertheless, like Hirayama, the Trichopoulos group published another paper in 1990, which appears to use methods nearly identical to those used in the first study; perhaps not surprisingly, it also reports a statistically significant increase* in lung cancer risk associated with marriage to a smoker.[29]

Questions about the reported findings of Hirayama and Trichopoulos, et al., were also prompted by their inconsistency with the conclusions of another study published that same year.

---

* A test for statistical significance permits an investigator to say that the results obtained in an investigation, in all probability, did not occur by chance. A statistically significant result also permits the investigator to say that the data in the study support rejection of the hypothesis that there is no association between ETS exposure and lung cancer in nonsmokers. A result which is <u>not</u> statistically significant, however, is consistent with the hypothesis that there is no effect. The data in such a study do not support rejection of the hypothesis that there is no association.

2023468947

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In late 1981, Lawrence Garfinkel, an official with the American Cancer Society (ACS), reported the results from a follow-up of the group's long-term lifestyle study, involving nearly 180,000 nonsmoking American women divided into categories based on the amount their husbands smoked.[30] By comparing the lung cancer mortality rates of women reportedly exposed to different levels of tobacco smoke, he determined that none of the differences observed were statistically significant and that "compared to nonsmoking women married to nonsmoking husbands, nonsmokers married to smoking husbands showed very little, if any, increased risk of lung cancer." Moreover, Garfinkel cautioned that any study which classified the wives' exposure to ETS solely upon the basis of their husbands' smoking habits could not account for the wives' total exposure and that, consequently, the results could be misleading. (For a discussion of somewhat different data from Garfinkel, see Garfinkel, et al., 1985, at p. 17 of this document.)

Although several subsequent studies have claimed to substantiate the reported findings of Hirayama and Trichopoulos, et al.,[31-36,38-39] a close examination of the methods and conclusions of these studies reveals that their claims are scientifically unfounded. For example, a report by Knoth, et al., which identified 39 nonsmoker lung cancer cases, asserted that exposure to ETS was the "most plausible explanation" for the reported lung cancers.[36] However, the study failed to provide a comparison group as a

2023468948

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

control population. One reviewer consequently characterized the report as containing "only tentative conclusions based on poor data analyzed by unacceptable methods."[37]

In a 1983 study, Correa, et al., reported finding an increased risk of lung cancer for nonsmokers married to smokers in the state of Louisiana in the southern United States.[38] However, the results were based on a small number of cases and did not take into account occupational and indoor and outdoor exposures or any other confounding variables. Furthermore, one of the co-authors of this study later issued reports with contradictory findings for a similar population in a neighboring state.[40-41]

The complex nature of the scientific data in this area is further illustrated by the mixed results of some studies; that is, certain data in a study may suggest a relationship between ETS and lung cancer while other data from the same study may not. For example, in a report on the preliminary results of a health survey conducted in two urban communities in Scotland, Gillis, et al., noted that of the six lung cancer deaths observed among male nonsmokers, four were in those who had reported exposure to ETS.[42] However, no dose-response relationship was noted for females in the study. In a follow-up study published in 1989, the authors provided additional data on lung cancer, as well as a number of other diseases and symptoms.[43] Although the additional data

2023468949

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

suggested a positive association between exposure to ETS and lung cancer in nonsmokers, the results were not statistically significant.

Kabat and Wynder, in a 1984 study in the United States of 25 male and 53 female nonsmoker lung cancer cases, reported a greater amount of ETS exposure at work for male cases compared to the controls.[44] However, no significant effect was reported for males exposed to ETS at home or for female cases exposed either at work or at home. Their conclusion for males was of marginal statistical significance; it is the only statistically significant result among the 11 studies in the published literature which have investigated workplace exposure.

In 1985, Garfinkel, et al., published a study of 134 nonsmoking women with lung cancer who were selected from hospital records during the period 1971 to 1981.[45] The paper provided two analyses of the same data which produced apparently contradictory results. While a statistically significant dose-response relationship was reported between nonsmoking female lung cancer patients and the number of cigarettes smoked per day by their spouses, no significant relationship was reported for the occurrence of lung cancer in nonsmoking women and the total number of hours per day of exposure to ETS over either the past five or 25 years.

2023468950

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In 1988, Shimizu, et al., reported elevated risks for lung cancer among nonsmoking Japanese women if either their mothers or fathers-in-law smoked, but "no association was observed" among nonsmoking wives of smokers who reported ETS exposures either at home or at work.[46]

In a 1988 case-control study of Chinese women, Geng, et al., reported a statistically significant association between lung cancer in nonsmoking women and spousal smoking. However, no significant associations were reported between lung cancer and exposure to ETS from parents or colleagues.[47]

Inoue and Hirayama reported the results of a case-control study on lung cancer in nonsmoking women from two cities in Japan.[48] The authors reported a marginally significant increased lung cancer risk among nonsmoking women whose husbands smoked more than 20 cigarettes per day. However, the data revealed no significant associations for lung cancer in relation to spousal smoking of less than 19 cigarettes per day, or for the overall category of "being married to a smoker."

In one of the most highly publicized articles in this area, U.S. researcher Dwight Janerich and his colleagues reported that household exposure of 25 or more "smoker years" during

2023468951

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

childhood and adolescence could double the risk of lung cancer for adult nonsmokers.[49] However, the study also noted that exposures to spousal smoking, smoking in the workplace, or smoking in social settings were not significantly associated with nonsmoker lung cancer incidence, nor were cumulative exposures during adulthood or over a lifetime. In a letter criticizing the study, British statistician and epidemiologist Peter Lee wrote: "To base conclusions on the single index that shows a marginally significant positive relation is a misrepresentation of findings from what is an essentially null study."[50] The study was also criticized for its failure to account fully for other confounding factors.[51-52] Additionally, the first report on this study, an unpublished doctoral or Ph.D. dissertation, did not even consider ETS exposure in childhood separately; it reported a statistically significant risk estimate only for 175 or more person/years of exposure.[53] (This number was calculated by multiplying the number of smokers in the household by the number of years nonsmokers spent living with them.) The Janerich, et al., study is the only one of nine published studies investigating childhood ETS exposure to report a statistically significant increase in risk.

Still other studies have reported no significant association between ETS and lung cancer. These include Chan and Fung's 1982 study from Hong Kong which reported fewer "passive smokers" among lung cancer patients than among controls.[54] The

2023468952

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

authors noted that "this finding is at variance with that of Dr. Hirayama's."

Similarly, Koo, et al., studied 200 female lung cancer cases among Chinese women and concluded that ETS exposure in the home or at work had no statistically significant impact on lung cancer incidence.[55] In a second study published three years later, this research group calculated total ETS exposures at home and at work for their population of nonsmoking female patients. They observed no significant disease trends for any of the lifetime measurements of exposure to ETS.[56]

In 1985, Wu, et al., using data from a study of female lung cancer cases in a large U.S. metropolitan area, reported that the lung cancer risk among the 31 nonsmokers in the study population was not affected by ETS exposure.[57]

Lloyd, et al., published results of a study undertaken to investigate the occurrence of lung cancer in an industrial area in Scotland.[58] The authors reported that ETS exposures were not significantly different between the cases and controls in the study; in other words, they reportedly found that ETS exposures appeared to play no role in the increased incidence of lung cancer in the study population.

2023468953

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Also in 1986, Lee and colleagues investigated the potential role of ETS on the incidence of nonsmoker lung cancer in England.[59] The researchers observed no significant trends in increased risk for lung cancer patients who reported exposure to ETS. In fact, in some disease categories, more controls than cases reported exposure to ETS.

Preliminary data from Geoffrey Kabat's on-going American Health Foundation study of 90 nonsmoker lung cancer cases, presented at a 1990 scientific meeting, indicate no statistically significant associations for lung cancer among males or females who were exposed to ETS during childhood or adulthood (in the home or the workplace).[60]

Sobue and colleagues, in a 1990 study of lung cancer among nonsmoking women in Osaka, Japan, reported no statistically significant associations between ETS exposures during childhood or adulthood and lung cancer among nonsmokers.[61] However, the researchers did note a statistically significant increased risk of lung cancer among women who had used wood or straw as cooking fuels.

In 1989, Swedish researchers Svensson, et al., assessed the relationship between ETS exposure and lung cancer among 38 never-smoking women.[62] They reported no statistically significant

2023468954

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

associations between lung cancer incidence and ETS exposures in childhood, in adulthood or over a lifetime.

The Wu-Williams, et al., study, published in 1990, is the largest Asian case-control study to date; it was conducted in two cities in northeast China by U.S. and Chinese researchers.[63] A statistically significant negative association was reported for spousal smoking and lung cancer in a sample of more than 200 lung cancer cases, suggesting that those women reporting exposures to ETS actually had a lower risk of lung cancer than those not exposed. Other lifestyle variables, e.g., use of coal-fired heating devices, traditional Chinese cooking practices, medical histories, and occupational exposures, were reported to be positively associated with lung cancer incidence.

Another study, conducted by Liu, He and Chapman in Xuanwei, China, reported no increase in lung cancer risk associated with ETS exposure, measured as the presence of a smoker in the household. A number of other factors, however, were reported to be associated with an increased risk for nonsmokers, including chronic bronchitis, family history of lung cancer and cooking over coal-burning stoves.[64-65]

In addition, relatively few studies have considered ETS exposures outside the home; only four studies sought information

2023468955

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

about total exposure to ETS from various sources.[45,55-56,59] Interestingly, none of these studies reported finding a significant association between total ETS exposure and lung cancer.

Meta-Analysis of ETS Studies

Perhaps as a result of the failure of most individual studies to report consistently significant results, certain researchers have recently begun using another method of statistical analysis which combines the reported results from numerous studies. With this method, called "meta-analysis," they claim to have calculated estimated excess risks for nonsmokers exposed to ETS that are 10 to 50 percent greater than those for nonexposed nonsmokers. In basic terms, they have reached these broad conclusions or "generalizations" by calculating an average of the relative risks for nonsmoker lung cancer cases reported by those studies.[66-70]

However, this method of generalization has been criticized for its questionable application to the epidemiological studies on ETS, due to their wide variety of study designs, population selections, techniques of analysis and results.[71-73] It also ignores basic methodologic weaknesses which, according to one governmental report, are characteristic of all the published studies on ETS and lung cancer.[74]

2023468956

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

This method further ignores the fact that the majority of the studies considered in the various meta-analyses do not report statistically significant increases in lung cancer risks for nonsmokers. For example, only two of the 13 studies considered by the 1986 NAS Report achieved statistical significance.[75] (Although the authors of several studies report risks which are not statistically significant, they report "positive" trends in their data. However, trends which fail the test for statistical significance cannot properly be characterized as disproving the null hypothesis or the hypothesis that there is no relationship between ETS exposures and lung cancer). Indeed, of the 29 studies on ETS and lung cancer in nonsmokers published to date, only six report statistically significant risk estimates for the exposure index of spousal smoking. In addition to considering flaws in the individual studies, it has been pointed out that meta-analyses themselves "should combine the careful thought and synthesis of a good review with the scientific rigor of a good experiment."[76]

The epidemiological studies on ETS cited in these meta-analyses were recently assessed by Letzel and coworkers for their scientific rigor; they also performed their own meta-analysis on the data pooled from those studies.[73] Of the 1,023 possible combinations of the 10 case-control studies they examined, only 24 gave rise to statistically significant results. Moreover, the

2023468957

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

statistical significance in those 24 combinations was dominated by the presence of three studies which have been described as of questionable scientific merit.[77] Letzel, et al., characterized the quality of the individual studies as "highly variable and sometimes poor."[28,73] They concluded that any computed excess risk would be negligible and, therefore, could not be used to support the claim that ETS exposures increase the risk of lung cancer in nonsmokers.

A critical review of meta-analysis as an analytic technique was published in 1990 by U.S. medical school researchers Fleiss and Gross.[78] In their review, they detailed the criteria for conducting an appropriate meta-analysis, and demonstrated that, when only U.S. studies of ETS and lung cancer were combined for reasons, among others, of homogeneity or similarity, a statistically nonsignificant summary risk estimate was calculated. Consequently, they concluded that "given the biases that exist in each individual study, the safest conclusion from the present meta-analysis is a negative one: There is no convincing scientific evidence from the epidemiological literature of an association between exposure to ETS and the risk of lung cancer in the U.S."

A similar conclusion was reached by U.S. statisticians Maxwell Layard and Maurice LeVois in their follow-up comments to the draft risk assessment on ETS and lung cancer issued by the U.S.

2023468958

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Environmental Protection Agency (EPA) in 1990.[79-80] The authors of the draft report performed a meta-analysis of 23 studies which resulted in a significant risk estimate for nonsmokers exposed to ETS. However, Layard and LeVois conducted an expanded meta-analysis, utilizing the EPA's methodology, that included three new studies which had appeared after the EPA staff prepared its document.[79] They calculated a summary relative risk which was "not statistically significant" and asserted that "the addition of the newly available epidemiology makes untenable the conclusion reached in the draft report concerning the ETS/nonsmoker lung cancer epidemiology."

Bias and Confounding Factors

The studies on ETS and lung cancer also have been criticized for their failure to account for a variety of biases and confounding factors that could affect the validity of their reported findings. In their discussion of such studies, for example, American researchers Ernst Wynder and Geoffrey Kabat cautioned that "if the observed relative risk is small," which they note is "the case" in the relationship between ETS and lung cancer, "it is important to determine whether the effect could be due to biased selection of subjects, confounding, biased reporting, or anomalies of particular subgroups."[81]

2023468959

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Statistician and epidemiologist Peter Lee has argued that the increased risks reported in the various meta-analyses are the result of an inherent bias in study design rather than the result of any genuine effect from exposure to ETS.[82-89] In his analyses, Lee has presented data which indicate that the reported risks cannot be explained on the basis of either ETS exposure or dose for the nonsmoker. Rather, he contends that the reported "risks" are the result of bias caused by a small number of smokers who are misclassified in the studies as nonsmokers.

Other kinds of misclassification may contribute to the reported increase in lung cancer risks among nonsmokers, according to several scientists. For example, none of the studies on ETS and lung cancer provides direct observational information on ETS exposures. Instead, spouses, next-of-kin or friends were asked to estimate the amount of ETS to which they thought the subject was exposed. Such estimates may result in what is called exposure misclassification,[90] which Garfinkel,[45] Friedman[91] and others[92-95] have reported leads to improper indices of exposure and incorrect estimations of risk. In Garfinkel's study, for example, the reported risk for lung cancer in the women exposed to ETS was actually less than for women not exposed when either the women's or their husbands' estimates were used.[45] Other authors, including the National Research Council, have recently criticized questionnaires used in ETS studies for not being standardized or

2023468960

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

validated; they pointed out that misclassification of exposure may occur if the questionnaire is not appropriately designed.[96-98]

Biostatistician Kilpatrick has identified another form of misclassification, called differential misclassification, which results "from the tendency of respondents to inflate the amount of ETS exposure for lung cancer cases and deflate the report of exposure for controls."[90] Similarly, Dr. Ernst Wynder, President of the American Health Foundation, notes that "relatives of a nonsmoking lung cancer patient are more likely to report passive inhalation exposure on the part of their relative than are relatives of a control patient."[99] Wynder and a co-author also noted that even if the patient herself is interviewed, some overreporting of ETS exposure may occur.[100]

Misclassification of case status can also arise if diagnoses of lung cancer are not histologically confirmed.[101] Without histologic confirmation, a tumor arising at another site and metastasizing or traveling to the lung could be erroneously identified as a primary lung tumor.

A more subtle form of potential bias, known as "publication bias," stems from the apparent unwillingness of scientific and medical journals to publish studies which report negative or weakly positive results.[71,102-103] Scientists have

2023468961

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

recently expressed concern over the growing trend among such journals to overemphasize (and hence to publish) only those studies which report positive increases in risk.[104-105] Published studies which are combined for meta-analyses, therefore, may not truly represent all investigations on the issue of ETS exposure and lung cancer.[106]

Moreover, most of the epidemiological studies on ETS and lung cancer have failed to consider age differences, diet, occupation and exposures to indoor or outdoor pollution as potential confounding elements. The importance of such factors is increasingly underscored in more recent publications.[107-108]

In developing countries, for example, the use of kerosene, gas, coal, liquefied petroleum gas, straw or wood for heating and cooking reportedly contributes to elevated levels of certain indoor air constituents, and may lead to increases in disease incidence.[109-110] Early, limited reports first suggested that exposures to indoor air constituents may be responsible for the increased risk of lung cancer among Oriental women.[111-112] Since then, a number of studies have reported elevated risks for lung cancer associated with the use of coal in stoves and other indigenous heating devices in China.[47,63-65,113-118] At least two papers have reported that certain cooking techniques which produce oil vapors, e.g., stir-frying and deep frying, were associated

2023468962

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

with increased lung cancer risks among Chinese women.[63,119] Another paper reported that national air quality standards were consistently exceeded in the Chinese kitchens studied.[120] Similarly, the use of kerosene, coal, wood or straw has been associated with an increased risk of lung cancer in Japanese women.[46,61] It appears that poor indoor air quality may not be restricted to Asian countries; similar observations regarding workplaces and offices have been made in Greece as well.[121]

In addition to poor indoor air quality from heating and cooking fuels, at least one epidemiologic study from northeast China reported statistically significant associations between outdoor air pollution and lung cancer incidence.[118]

Several aspects of diet have been suggested to be possible confounding factors. For instance, Dr. Linda Koo, in several papers published between 1988 and 1990, re-analyzed her data on nonsmoking wives of smokers.[122-125] Her results indicated that wives of nonsmoking husbands had "healthier" lifestyles than wives of smoking husbands; they exhibited higher socio-economic status and had better indices of family cohesiveness and lower frequencies of selected health problems and complaints. An important and statistically significant difference was reportedly found in the diets of the two groups. Wives of smoking husbands consumed more processed and spicy foods and ate fewer fresh fruits and vegetables than

2023468963

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

wives of nonsmoking men. Koo concluded that such correlates of smoking status "act as important confounders when evaluating health risks among families with smoking husbands." She also wrote:

> [C]aution should be exercised when interpreting data on ETS. It may not be the hazards of tobacco smoke that are being evaluated, but a whole range of behaviors that result from having a smoking husband, which may in turn increase the risk for certain diseases among their wives and children.[122]

Moreover, in 1989, Sidney and colleagues reported that nonsmokers living with smokers consumed less carotene (Vitamin A) than nonsmokers who lived with other nonsmokers. They concluded that "dietary beta-carotene intake is a potential confounder and should be measured whenever possible in studies of the relation between passive smoking and lung cancer."[126] In 1991, additional supportive data were provided by Le Marchand and colleagues' study of women in Hawaii, which found that beta-carotene intake was inversely associated with ETS exposure.[127] The authors noted: "Decreased beta-carotene consumption could explain, in part or in total, the moderately elevated lung-cancer risk observed for passive smokers in past studies." In addition, in a 1990 abstract, Waller and Smith reported a correlation between serum beta-carotene level and socioeconomic status, suggesting that the relationship may be even more complex.[128] Another aspect of diet, namely, consumption of green tea, was associated with a statistically significant

2023468964

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

increased risk of lung cancer in women in Hong Kong.[129] Similar results were first reported at a 1987 conference in Tokyo, in a paper calling for increased attention to possible relationships between substances taken in orally and lung cancer.[130]

Other potential confounders in studies of ETS and lung cancer include occupational exposures;[46-47,63,118,131] personal health factors (e.g., menstrual cycle length, history of respiratory disease);[47,63,65,121] family history of lung cancer;[63,65] and even keeping pet birds.[132]

Swedish scientist Ragnar Rylander summed up the importance of confounders in a 1990 article.[108] He cautioned that studies evaluating the relationship between exposure to ETS and lung cancer "must take into account other environmental risk or protection factors and the possibility that exposure to environmental tobacco smoke may be confounded," which he noted "has not been considered in the majority of such studies." He concluded: "Until this has been done, the claim of causality between environmental tobacco smoke and lung cancer remains uncertain."

Mathematical Models

In 1985, Repace and Lowrey, two antismoking advocates, published an article in which they estimated that exposure to ETS

2023468965

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

is responsible for 500 to 5,000 lung cancer deaths a year among nonsmokers in the United States.[133] The risk estimates were cited widely in the press prior to the article's publication, perhaps because it was incorrectly identified as a study by the EPA. In reality, the article was neither approved nor endorsed by that agency.

The article itself presents two highly theoretical models for estimating risks of lung cancer from ETS exposures. The first model relies upon a "reinterpretation" of the epidemiological studies of lung cancer in nonsmokers, and the second provides an estimate for lung cancer mortality derived from data in a study of Seventh Day Adventists, a religious group known for its vigorous opposition to smoking.

Critics of the latter approach have pointed out that the estimates are based on errors and "unrealistic assumptions" which result in overestimations of exposure.[134-135] For example, one recent analysis of the Seventh Day Adventist model showed that, depending upon the assumptions and data used, such model estimates are inherently inaccurate and may vary by as much as 300-fold.[136] Another scientist noted that the exposure and dose levels they used are not based on actual measurements, and that actual measurements reported by other researchers range from "ten-to-one-hundred-fold less than that in the Repace and Lowrey

2023468966

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

model."[137] Still other scientists have questioned both methods of analysis used in their article.[138-140] They suggest that Repace and Lowrey failed to control for other confounding factors, and that their model did not provide "the very statistical bases of estimation procedures."[137]

Repace and Lowrey's estimate of nonsmoker lung cancer risks in the workplace has been criticized by another group of scientists who pointed out that none of the epidemiological studies which examined the relationship between ETS exposure in the workplace and disease in nonsmoking women report a statistically significant increase in risk.[134] Repace and Lowrey have failed to address these criticisms, and, in fact, published a similar article in 1990, in which they conclude that 5,000 (plus or minus 2,400) lung cancer deaths are due to ETS each year.[141]

In 1988, British researchers Darby and Pike published a paper describing another type of mathematical model which purportedly can be used to predict potential effects from ETS exposure based on data from a study of active smoking.[142] However, even after adjusting for childhood exposure to ETS, the authors noted that the predicted risk for nonsmokers was smaller than "the underlying background risk of lung cancer," and that their model could not explain the difference between risks reported for nonsmokers in epidemiological studies and the low levels of ETS

2023468967

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

exposure reported in other types of studies. When the validity of their model was challenged,[143] they replied that the existing data for the indicator of ETS exposure they utilized were insufficient and inappropriate for making comparisons between the epidemiologic and extrapolation approaches to risk assessment.[144]

Summary

Attempts to generate statistically significant results from epidemiological studies on ETS and nonsmoker lung cancer are unconvincing, due to scientific deficiencies in each of the studies.[145] A German specialist in biometrics and epidemiology, in his assessment of these studies, has explained why the data fail to meet the criteria which some regard as necessary to establish a causal relationship:

> The majority of criteria for a causal connection are not fulfilled. There is no consistency, there is a weak association, there is no specificity, the dose-effect relation can be viewed controversially, bias and confounding are not adequately excluded, there is no intervention study, significance is only present under special conditions and the biologic plausibility can be judged controversially.[145]

Given these difficulties in interpretation, it is therefore not surprising that an eminent statistician has observed:

2023468968

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

> [I]t is unlikely that any epidemiological study has been, or can be, conducted which could permit establishing that the risk of lung cancer has been raised by passive smoking. Whether or not the risk is raised remains to be taken as a matter of faith according to one's choice.[102]

This same statistician concluded: "What with subtle biases, not so subtle biases, and even extravagant errors, one should not accept too readily claimed demonstrations of ill effects of passive smoking."[72]

Overall Mortality and Cancer Other Than the Lung

A few articles have claimed that the risk for all cancers is higher among nonsmokers exposed to ETS. One such study by Miller examined a population which was selected from death notices in a northeastern U.S. newspaper.[146-147] However, analysis of the data reveals that the reported risk disappears when age comparisons of cases and controls are considered.[148]

In a series of papers based on data of cancer cases selected from a North Carolina hospital tumor registry, Sandler, et al., reported increased risks for lung cancer and cancer of other sites in nonsmokers exposed to ETS.[149-151] Yet, published criticisms cast serious doubt on these conclusions. One commentator challenged the authors' selection of controls and their use of

2023468969

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

questionnaire information.[152] Another scientist observed that under one interpretation, the data suggest that exposure to ETS had no effect on overall cancer incidence.[153-154] A third critic called the studies "seriously flawed" and questioned the authors' methods of data collection.[155] Still others challenged their conclusions because the reports had not considered potential confounding variables such as diet, hygiene and lifestyle.[156-157]

In 1989, Sandler, et al., evaluated mortality from all causes for nonsmokers in a Maryland county. Although the authors reported slightly higher risks for nonsmokers who lived with smokers than for those who lived with nonsmokers, they acknowledged that "these small nonspecific increases in death rates may reflect other characteristics of passive smokers that increase mortality."[158] This paper was also strongly criticized by a reviewer who wrote that it should have been rejected for publication "on the basis that it is poor science and inadequately designed and undertaken to address the issue presented in the title."[159]

A. Judson Wells, in a 1988 publication, estimated that in the United States thousands of nonsmoker deaths from all causes could be attributed to exposure to ETS.[160] Yet even the editor of the journal which published his paper reported that one pre-publication reviewer had recommended that the paper not be published because it was "too speculative."[161] Three critical responses were

2023468970

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

published in 1990,[107,162-163] one of which called Wells' estimates "scientifically unjustified."[107] However, Repace and Lowrey praised Wells' work, and Wells himself attacked the three critical commenters, although he failed to address the issues they raised.[164-165]

With regard to the issue of ETS and overall mortality, Vandenbroucke and colleagues' 25-year follow-up study of over 1,000 married couples in Holland reported that "passive smoking was not associated with an increase in total mortality."[166] Although the authors cautioned that the results do not necessarily contradict those which suggest such an association, they added that their findings "were reassuring to the extent that the possible absolute risk carried by passive smoking is probably small."

Only a few studies have considered ETS exposure and cancer of individual, non-pulmonary, sites. In 1989, Slattery and colleagues reported an increased risk of cervical cancer in nonsmoking women who reported three or more hours of ETS exposure per day.[167-168] However, the study was strongly criticized for its failure to account for all pertinent confounding variables.[169] Kabat, et al., and Burch, et al., have independently investigated bladder cancer incidence and ETS exposure;[170-171] neither study reported an association between bladder cancer and exposure to ETS at home or at work.

2023468971

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Two studies, by John, et al., and Grufferman, et al., have suggested that there may be an association between childhood ETS exposure (particularly paternal smoking) and the incidence of certain childhood cancers; however, both studies involved very small numbers of cases.[172-173] Finally, isolated reports have claimed that their data support an association between ETS exposure and brain and nasal sinus cancers,[1] or breast cancer.[1,149] Without adequate replication of these results, it is not possible to reach any definitive conclusion about ETS exposure and non-pulmonary cancer incidence.

A presenter at a 1989 scientific symposium in Montreal, Canada, who had reviewed many of these studies, contended that the studies available at that time provided "insufficient data to evaluate the effect of ETS on cancer other than of the lung."[174] He also asserted that the studies had numerous shortcomings: "The reported associations are weak and inconsistent, and are subject to the potential effects of biases and uncontrolled confounding factors . . . ."

2023468972

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Lung Cancer

1. Hirayama, T., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer: A Study from Japan," British Medical Journal 282: 183-185, 1981.

2. Trichopoulos, D., Kalandidi, A., Sparros, L. and MacMahon, B., "Lung Cancer and Passive Smoking," International Journal of Cancer 27(1): 1-4, 1981.

3. Adlkofer, F., "Probleme mit dem Passivrauchen (The Problems of Passive Smoking)," Der Kassenarzt 27(51/52): 29-39, 1987. Translation.

4. Ahlborn, W. and Uberla, K., "Passive Smoking and Lung Cancer: Reanalyses of Hirayama's Data." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 169-178, 1988.

5. Uberla, K. and Ahlborn, W., "Passive Smoking and Lung Cancer: A Reanalysis of Hirayama's Data." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 333-340, 1990.

6. Aviado, D., "Toxicological Basis for Regulation of Indoor Air Quality," Journal of Applied Toxicology 8(3): 155-157, 1988.

7. Diamond, G. and Forrester, J., "Clinical Trials and Statistical Verdicts: Probable Grounds for Appeal," Annals of Internal Medicine 98(3): 385-394, 1983.

8. Gostomzyk, J., "Krank durch Passivrauchen? (Disease Due to Passive Smoking?)," Münch med Wschr 124(4): 11, 1982. Translation.

9. Grimmer, G., "Kausalitatsbeziehung Fraglich (Causality-Relationship Questionable)," Münch med Wschr 124(4): 16, 1982. Translation.

10. Grundmann, E., Mueller, K.-M. and Winter, K.D., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer," British Medical Journal 282(6270): 1156, 1981.

11. Kilpatrick, S.J. and Viren, J., "Age as a Modifying Factor in the Association Between Lung Cancer in Non-Smoking Women and Their Husbands' Smoking Status." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 195-202, 1988.

2023468973

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

12. Kilpatrick, S.J., "An Example of Extra-Poisson Variation Suggesting an Under-Specified Model." In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois and M. Govaerts (eds.). Amsterdam, Excerpta Medica, 83-90, 1989.

13. Kilpatrick, S.J., "Model Specification Effects in ETS/Nutrition Research." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 256-271, 1990.

14. Lee, P.N., "Passive Smoking," Food Chemistry and Toxicology 20: 223-229, 1982.

15. Lehnert, G., "Schlusswort: Zum Bereich des Spekulativen (Conclusion: In the Realm of Speculation)," Münch med Wschr 124(4): 19-20, 1982. Translation.

16. MacDonald, E.J., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer," British Medical Journal 283: 915-916, 1981.

17. MacDonald, E.J., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer," British Medical Journal 283(6304): 1465, 1981.

18. Mantel, N., "Epidemiologic Investigations: Care in Conduct, Care in Analysis, and Care in Reporting," Journal of Cancer Research and Clinical Oncology 105: 113-116, 1983.

19. Rutsch, M., "Mangelhafte Statistische Absicherung (Inadequate Statistical Substantiation)," Münch med Wschr 124(4): 15, 1982. Translation.

20. Rutsch, M., "Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer," British Medical Journal 282: 985, 1981.

21. Schievelbein, H., "Kein Beweis fur Gesundheitsschadlichkeit (No Proof for Injuriousness to Health)," Münch med Wschr 124(4): 13-15, 1982. Translation.

22. Schmahl, D., Quoted in "Lungenkrebs durch Passivrauchen? Studie aus Japan bestatigt Verdacht/Widerspruch aus Deutschland (Lung Cancer from Passive Smoking? Study from Japan Confirms Suspicion/Contradictory Opinion from Germany)," by J. Troger, Suddeutsch Zeitung, March 18, 1981. Translation.

23. Sterling, T.D., "Non-Smoking Wives of Heavy Smokers Have a High Risk of Lung Cancer," British Medical Journal 282: 1156, 1981.

2023468974

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

24. Rylander, R., "Environmental Tobacco Smoke and Lung Cancer." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Disease, Supplement 133, Volume 65, 127-133, 1984.

25. Schneider, B., "Risk Assessment for Inhomogeneous Subgroups." In: Assessment of Inhalation Hazards. U. Mohr (ed.). Berlin, Heidelberg, Springer-Verlag, 285-291, 1989.

26. Hirayama, T., Life-Style and Mortality: A Large-Scale Census-Based Cohort Study in Japan. Contributions to Epidemiology and Biostatistics, Vol. 6. Basel, Karger, 1990.

27. Trichopoulos, D., Kalandidi, A. and Sparros, L., "Lung Cancer and Passive Smoking: Conclusion of Greek Study," Lancet II: 677-678, 1983.

28. Letzel, H. and K. Uberla, "Meta-Analyses on Passive Smoking and Lung Cancer." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 316-322, 1990.

29. Kalandidi, A., Katsouyanni, K., Voropoulou, N., Bastas, G., Saracci, R. and Trichopoulos, D., "Passive Smoking and Diet in the Etiology of Lung Cancer Among Non-Smokers," Cancer Causes and Control 1: 15-21, 1990.

30. Garfinkel, L., "Time Trends in Lung Cancer Mortality Among Nonsmokers and a Note on Passive Smoking," Journal of the National Cancer Institute 66(6): 1061-1066, 1981.

31. Lam, T.H., Kung, I.T.M., Wong, C.M., Lam, W.K., Kleevens, J.W.L., Saw, D., Hsu, C., Seneviratne, S., Lam, S.Y., Lo, K.K. and Chan, W.C., "Smoking, Passive Smoking and Histological Types in Lung Cancer in Hong Kong Chinese Women," British Journal of Cancer 56(5): 673-678, 1987.

32. Pershagen, G., Hrubec, Z. and Svensson, C., "Passive Smoking and Lung Cancer in Swedish Women," American Journal of Epidemiology 125(1): 17-24, 1987.

33. Akiba, S., Kato, H. and Blot, W.J., "Passive Smoking and Lung Cancer Among Japanese Women," Cancer Research 46: 4804-4807, 1986.

34. Humble, C.G., Samet, J.M. and Pathak, D.R., "Marriage to a Smoker and Lung Cancer Risk," American Journal of Public Health 77(5): 598-602, 1987.

2023468975

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

35. Brownson, R.C., Reif, J.S., Keefe, T.J., Ferguson, S.W. and Pritzl, J.A., "Risk Factors for Adenocarcinoma of the Lung," American Journal of Epidemiology 125(1): 25-34, 1987.

36. Knoth, A., Bohn, H. and Schmidt, F., "Passive Smoking as a Causative Factor of Lung Cancer in Nonsmoking Women," Med Klin Prax 78(2): 56-59, 1983. Translation.

37. Heller, W., "Lung Cancer and Passive Smoking," Lancet II: 1309, 1983.

38. Correa, P., Pickle, L.W., Fontham, E., Lin, Y. and Haenszel, W., "Passive Smoking and Lung Cancer," Lancet II: 595-597, 1983.

39. Lam, W.K., A Clinical and Epidemiological Study of Carcinoma of Lung in Hong Kong, M.D. Thesis Submitted to the University of Hong Kong, 1985.

40. Buffler, P.A., Pickle, L.W., Mason, T.J. and Contant, C., "The Causes of Lung Cancer in Texas." In: Lung Cancer: Causes and Prevention. M. Mizell and P. Correa (eds.). Deerfield Beach, Verlag Chimie International, 83-99, 1984.

41. Shaw, G.L., Falk, R.T., Pickle, L.W., Mason, T.J. and Buffler, P.A., "Lung Cancer Risk Associated With Cancer in Relatives," Journal of Clinical Epidemiology 44(4/5): 429-437, 1991.

42. Gillis, C.R., Hole, D.J., Hawthorne, V.M. and Boyle, P., "The Effect of Environmental Tobacco Smoke in Two Urban Communities in the West of Scotland." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Disease, Supplement 133, Volume 65, 121-126, 1984.

43. Hole, D.J., Gillis, C.R., Chopra, C. and Hawthorne, V.M., "Passive Smoking and Cardiorespiratory Health in a General Population in the West of Scotland," British Medical Journal 299: 423-427, 1989.

44. Kabat, G. and Wynder, E., "Lung Cancer in Nonsmokers," Cancer 53(5): 1214-1221, 1984.

45. Garfinkel, L., Auerbach, O. and Joubert, L., "Involuntary Smoking and Lung Cancer: A Case-Control Study," Journal of the National Cancer Institute 75(3): 463-469, 1985.

46. Shimizu, H., Morishita, M., Mizuno, K., Masuda, T., Ogura, Y., Santo, M., Nishimura, M., Kunishima, K., Karasawa, K.,

2023468976

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Nishiwaki, K., Yamamoto, M., Hisamichi, S. and Tominaga, S., "A Case-Control Study of Lung Cancer in Nonsmoking Women," Tohoku Journal of Experimental Medicine 154: 389-97, 1988.

47. Geng, G.-Y., T.H. Liang, A.Y. Zhang and G.L. Wu, "On the Relationship Between Smoking and Female Lung Cancer." In: Smoking and Health 1987. M. Aoki, S. Hisamichi and S. Tominaga (eds.). Amsterdam, Excerpta Medica, 483-486, 1988.

48. Inoue, R. and Hirayama, T., "Passive Smoking and Lung Cancer in Women." In: Smoking and Health 1987. M. Aoki, S. Hisamichi and S. Tominaga (eds.). Amsterdam, Excerpta Medica, 283-285, 1988.

49. Janerich, D., Thompson, W.D., Varela, L.R., Greenwald, P., Chorost, S., Tucci, C., Zaman, M.B., Melamed, M.R., Kiely, M. and McKneally, M.F., "Lung Cancer and Exposure to Tobacco Smoke in the Household," New England Journal of Medicine 323: 632-636, 1990.

50. Lee, P., "Correspondence: Lung Cancer and Exposure to Tobacco Smoke in the Household," New England Journal of Medicine 324(6): 412-413, 1991.

51. van Poppel, G., Kor, F.J., Gorolls, W.J.M.J. and Schrijver, J., "Correspondence: Lung Cancer and Exposure to Tobacco Smoke in the Household," New England Journal of Medicine 324(6): 413-414, 1991.

52. Sterling, T.D. and Weinkam, J.J., "Correspondence: Lung Cancer and Exposure to Tobacco Smoke in the Household," New England Journal of Medicine 324(6): 414, 1991.

53. Varela, L., "Assessment of the Association Between Passive Smoking and Lung Cancer," Ph.D. Dissertation, Yale University, 1987.

54. Chan, W. and S. Fung, "Lung Cancer in Non-Smokers in Hong Kong." In: Cancer Campaign Vol. 6, Cancer Epidemiology. E. Grundmann (ed.). Stuttgart, Gustav Fischer Verlag, 199-202, 1982.

55. Koo, L.C., Ho, J.H.-C. and Saw, D., "Is Passive Smoking an Added Risk Factor for Lung Cancer in Chinese Women?," Journal of Experimental and Clinical Cancer Research 3(3): 277-283, 1984.

56. Koo, L.C., Ho, J.H.-C., Saw, D. and Ho., C.Y., "Measurements of Passive Smoking and Estimates of Lung Cancer Risk Among

2023468977

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Non-Smoking Chinese Females," International Journal of Cancer 39: 162-169, 1987.

57. Wu, A., Henderson, B.E., Pike, M.C. and Yu, M.C., "Smoking and Other Risk Factors for Lung Cancer in Women," Journal of the National Cancer Institute 74(4): 747-751, 1985.

58. Lloyd, O.L., Ireland, E., Tyrrell, H. and Williams, F., "Respiratory Cancer in a Scottish Industrial Community: A Retrospective Case-Control Study," Journal of the Society for Occupational Medicine 36: 2-8, 1986.

59. Lee, P.N., Chamberlain, J. and Alderson, M.R., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," British Journal of Cancer 54: 97-105, 1986.

60. Kabat, G.C., "Epidemiologic Studies of the Relationship Between Passive Smoking and Lung Cancer." In: Toxicology Forum: 1990 Annual Winter Meeting. Washington, D.C., 187-199, February 19-21, 1990.

61. Sobue, T., Suzuki, R., Nakayama, N., Inubuse, C., Matsuda, M., Doi, O., Mori, T., Furuse, K., Fukuoka, M., Yasumitsu, T., Kuwabara, O., Ichigaya, M., Kurata, M., Kuwabara, M., Nakahara, K., Endo, S. and Hattori, S., "Passive Smoking Among Nonsmoking Women and the Relationship Between Indoor Air Pollution and Lung Cancer Incidence -- Results of a Multicenter Case Controlled Study," Gan to Rinsho 36(3): 329-333, 1990. Translation.

62. Svensson, C., Pershagen, G. and Klominek, J., "Smoking and Passive Smoking in Relation to Lung Cancer in Women," Acta Oncologica 28(5): 623-639, 1989.

63. Wu-Williams, A.H., Dai, X.D., Blot, W., Xu, Z.Y., Sun, X.W., Xiao, H.P., Stone, B.J., Yu, S.F., Feng, Y.P., Ershow, A.G., Sun, J., Fraumeni, J.F and Henderson, B.E., "Lung Cancer Among Women in North-East China," British Journal of Cancer 62: 982-987, 1990.

64. He, X., Chen, W., Liu, Z. and Chapman, R.S., "An Epidemiological Study of Lung Cancer in Xuan Wei County, China: Current Progress," Archives of Environmental Health 46(2): 118-119, 1991. Abstract.

65. Liu, Z., He, X. and Chapman, R.S., "Smoking and Other Risk Factors for Lung Cancer in Xuanwei, China," International Journal of Epidemiology 20(1): 26-31, 1991.

2023468978

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

66. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

67. Wald, N.J., Nanchahal, K., Thompson, S.G. and Cuckle, H.S., "Does Breathing Other People's Tobacco Smoke Cause Lung Cancer?," British Medical Journal 293: 1217-1222, 1986.

68. Blot, W.J. and Fraumeni, J.F., "Passive Smoking and Lung Cancer," Journal of the National Cancer Institute 77(5): 993-100, 1986.

69. Doll, R., "Lung Cancer: Observed and Expected Changes in Incidence from Active and Passive Smoking," Presentation to The International Union AGainst Cancer (UICC) Conference, Budapest, Hungary, August, 1986.

70. Zmirou, D., Blatier, J.F., Andre, E., Ferley, J.P., Balducci, F., Rossum, F. and Delormas, P., "Passive Smoking and Respiratory Risk: A Quantitative Synthesis of the Literature," Rev Mal Respir 4: 361-371, 1990. Translation.

71. Katzenstein, A., Environmental Tobacco Smoke (ETS) and Risk of Lung Cancer -- How Convincing is the Evidence?, Larchmont, New York, Katzenstein Associates, March, 1987.

72. Mantel, N., "What Is the Epidemiologic Evidence for a Passive Smoking-Lung Cancer Association?" In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 341-347, 1990.

73. Letzel, H., Blumner, E. and Uberla, K., "Meta-Analyses on Passive Smoking and Lung Cancer: Effects of Study Selection and Misclassification of Exposure." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 293-302, 1988.

74. Office of Technology Assessment, Special Projects Office of the Health Program, Staff Paper, Passive Smoking in the Workplace: Selected Issues, United States Congress, May, 1986.

75. Schwartz, S.L. and Balter, N.J., "ETS-Lung Cancer Epidemiology: Supportability of Misclassification and Risk Assumptions." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 159-168, 1988.

2023468979

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

76. Goodman, S.N., "Have You Ever Meta-Analysis You Didn't Like?," Annals of Internal Medicine 114(3): 244-246, 1991.

77. Brown, R.C., "Environmental Tobacco Smoke in the Context of Indoor Air Quality," Human Toxicology 8: 3-4, 1989.

78. Fleiss, J.L. and Gross, A.J., "Meta-Analysis in Epidemiology, with Special Reference to Studies of the Association Between Exposure to Environmental Tobacco Smoke and Lung Cancer: A Critique," Journal of Clinical Epidemiology 44(2): 127-139, 1991.

79. Layard, M.W. and LeVois, M.E., Letter to D.G. Barnes, Director of Science Advisory Board, U.S. Environmental Protection Agency, April 9, 1991.

80. U.S. Environmental Protection Agency, Office of Health and Environment Assessment, Office of Atmospheric and Indoor Air Programs, Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA 600/6-90/006A, May, 1990.

81. Wynder, E.L. and Kabat, G.C., "Environmental Tobacco Smoke and Lung Cancer: A Critical Assessment." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 5-15, 1990.

82. Lee, P., "Passive Smoking and Lung Cancer: Problems in Interpreting the Epidemiological Data," Presentation to the Toxicology Forum, Washington, D.C., February, 1987.

83. Lee, P., "Does Breathing Other People's Tobacco Smoke Cause Lung Cancer?," British Medical Journal 293: 1503-1504, 1986.

84. Lee, P., "Misclassification as a Factor in Passive Smoking Risk," Lancet 2(8511): 867, 1986.

85. Lee, P., "Lung Cancer and Passive Smoking: Association or Artefact Due to Misclassification of Smoking Habits?," Toxicology Letters 35: 157-162, 1987.

86. Lee, P., "Passive Smoking and Lung Cancer Association: A Result of Bias?," Human Toxicology 6: 517-524, 1987.

87. Lee, P., "An Alternative Explanation for the Increased Risk of Lung Cancer in Non-Smokers Married to Smokers." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 149-158, 1988.

2023468980

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

88. Lee, P., "Passive Smoking and Lung Cancer: Fact or Fiction?" In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois and M. Govaerts (eds.). Amsterdam, Elsevier Science Publishers, 119-128, 1989.

89. Lee, P.N., "Increased Risk of Lung Cancer in Non-Smokers Married to Smokers: A Result of ETS Exposure or of Bias?," In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 25-36, 1990.

90. Kilpatrick, S., "Misclassification of Environmental Tobacco Smoke Exposure: Its Potential Influence on Studies of Environmental Tobacco Smoke and Lung Cancer," Toxicology Letters 35: 163-168, 1987.

91. Friedman, G., Petitti, D.B. and Bawol, R.D., "Prevalence and Correlates of Passive Smoking," American Journal of Public Health 73(4): 401, 1983.

92. Pron, G.E., Burch, J.D., Howe, G.R. and Miller, A.B., "The Reliability of Passive Smoking Histories Reported in a Case-Control Study of Lung Cancer," American Journal of Epidemiology 127(2): 267-273, 1988.

93. Schenker, M., Hammond, K., Samuels, S.,·Kado, N. and Woskie, S., "Assessment of Environmental Tobacco Smoke Exposure in Epidemiologic Studies," Chest 91(2): 313-314, 1987. Abstract.

94. Lerchen, M.L. and Samet, J.M., "An Assessment of the Validity of Questionnaire Responses Provided by a Surviving Spouse," American Journal of Epidemiology 123(3): 481-489, 1986.

95. Sandler, D.P. and Shore, D.L., "Quality of Data on Parents' Smoking and Drinking Provided by Adult Offspring," American Journal of Epidemiology 124(5): 768-778, 1986.

96. Leaderer, B., "Assessing Exposures to Environmental Tobacco Smoke," Risk Analysis 10(1): 19-26, 1990.

97. Shimizu, Y., Namekata, T. and Takemoto, K., "Epidemiological Issues on Involuntary Smoking and Lung Cancer." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 323-332, 1990.

98. National Research Council, National Academy of Sciences, "Current and Anticipated Applications." In: Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities. Washington, D.C., National Academy Press, 207-218, 1991.

2023468981

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

99. Wynder, E., "Guidelines to the Epidemiology of Weak Associations," Preventive Medicine 16: 211-212, 1987.

100. Wynder, E. and Kabat, G., "Health Care and Society: Environmental Tobacco Smoke and Lung Cancer." In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois and M. Govaerts (eds.). Amsterdam, Elsevier Science Publishers, 135-145, 1989.

101. Faccini, J.M., "The Role of Histopathology in the Evaluation of Risk of Lung Cancer from Environmental Tobacco Smoke," Experimental Pathology 37: 177-180, 1989.

102. Mantel, N., "Lung Cancer and Passive Smoking," British Medical Journal 294: 440, 1987.

103. Lee, P., "Deaths in Canada from Lung Cancer Due to Involuntary Smoking," CMAJ 137: 372-373, 1987.

104. Gordis, L., "Challenges to Epidemiology in the Next Decade," American Journal of Epidemiology 128(1): 1-9, 1988.

105. Newcombe, R.G., "Towards a Reduction in Publication Bias," British Medical Journal 295: 656-659, 1987.

106. Buffler, P.A., "The Evaluation of Negative Epidemiologic Studies: The Importance of All Available Evidence in Risk Characterization," Regulatory Toxicology and Pharmacology 9: 34-43, 1989.

107. Katzenstein, A.W., "An Estimate of Adult Mortality in the United States from Passive Smoking: A Response," Environment International 16: 175-178, 1990.

108. Rylander, R., "Environmental Tobacco Smoke and Lung Cancer," The New England Journal of Medicine 323(12): 834, 1990.

109. Chen, B.H., Hong, C.J., Pandey, M.R. and Smith, K.R., "Indoor Air Pollution in Developing Countries," World Health Statistics Quarterly 43: 127-138, 1990.

110. Anonymous, "Indoor Air Pollution in Developing Countries," Lancet 336(8730): 1548, 1990.

111. deSerres, F. and T. Matsushima, "Meeting Report: Mutagenesis and Carcinogenesis by Nitropyrenes and Cancer Chemotherapeutics," Mutation Research 164: 4, 1986.

112. Anonymous, "Lung Cancer in South China," Oncology Times, 8(6): 33, 1986.

2023468982

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

113. Mumford, J.L., He, X.Z., Chapman, R.S., Cao, S.R., Harris, D.B., Li, X.M., Xian, Y.L., Jiang, W.Z., Xu, C.W., Chuang, J.C., Wilson, W.E. and Cooke, M., "Lung Cancer and Indoor Air Pollution in Xuan Wei, China," Science 235: 217-220, 1987.

114. Chapman, R.S., Mumford, J.L., Harris, D.B., He, X., Jiang, W. and Yang, R., "The Epidemiology of Lung Cancer in Xuan Wei, China: Current Progress, Issues and Research Strategies," Archives of Environmental Health 43(2): 180-185, 1988.

115. Wang, F.-L., et al., "Analysis of Risk Factors for Female Lung Cancer in Haerbin: Indoor Air Pollution," Chinese Journal of Preventive Medicine 23(5): 270-273, 1989.

116. Du, Y.-X. and X.-L. Ou, "Indoor Air Pollution and Woman Lung Cancer." In: Indoor Air '90: Proceedings of the 5th International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 59-64, July 29-August 3, 1990.

117. He, F., "Health Effects of Indoor Air Pollution by Coal Combustion in China." In: Indoor Air Quality and Ventilation. London, Selper, Ltd., 305-311, 1990.

118. Xu, Z.-Y., Blot, W.J., Xiao, H.-P., Wu, A., Feng, Y.-P., Stone, B.J., Sun, J., Ershow, A.G., Henderson, B.E. and Fraumeni, J.F., "Smoking, Air Pollution, and the High Rates of Lung Cancer in Shenyang, China," Journal of the National Cancer Institute 81: 1800-1806, 1989.

119. Gao, Y.-T., Blot, W.J., Zheng, W., Ershow, A.G., Hsu, C.W., Levin, L.I., Zhang, R. and Fraumeni, J.F., "Lung Cancer Among Chinese Women," International Journal of Cancer 40: 604-609, 1987.

120. Bu, W., "Ventilation and Its Effects on Pollution in Chinese Kitchens." In: Indoor Air Quality and Ventilation. London, Selper, Ltd., 129-132, 1990.

121. Bazas, B., "An Overview of Indoor Air Quality in Certain Greek Industries, Workshops and Offices." In: Indoor Air Quality and Ventilation. London, Selper, Ltd., 237-240, 1990.

122. Koo, L.C., Ho, J.H.-C. and Rylander, R., "Life-History Correlates of Environmental Tobacco Smoke: A Study on Nonsmoking Hong Kong Chinese Wives with Smoking Versus Nonsmoking Husbands," Soc Sci Med 26(7): 751-760, 1988.

2023468983

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

123. Koo, L., "Dietary Habits and Lung Cancer Risk Among Chinese Females in Hong Kong Who Never Smoked," Nutrition and Cancer 11: 155-172, 1988.

124. Koo, L.C., "Environmental Tobacco Smoke and Lung Cancer: Is It the Smoke or the Diet?" In: Present and Future of Indoor Air Quality. C.J. Bieva, Y.Courtois and M. Govaerts (eds.). Amsterdam, Elsevier Science Publishers, 65-75, 1989.

125. Koo, L.C. and J.H.-C. Ho, "Is There a Threshold Effect for ETS? Results of Data from Chinese Females Who Had Never Smoked." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 290-298, 1990.

126. Sidney, S., B.J. Caan and G.D. Friedman, "Daily Intake of Carotene in Nonsmokers With and Without Passive Smoking at Home," American Journal of Epidemiology 129(6): 1305-1309, 1989.

127. Le Marchand, L., Wilkens, L.R., Hankin, J.H. and Haley, N.J., "Dietary Patterns of Female Nonsmokers With and Without Exposure to Environmental Tobacco Smoke," Cancer Causes and Control 2: 11-16, 1991.

128. Waller, K.D. and A.H. Smith, "Effects of Socioeconomic Status and Smoking on Serum Beta-Carotene," Archives of Environmental Health 46(2): 120, 1991.

129. Tewes, F.J., Koo, L.C., Meisgen, T.J. and Rylander, R., "Lung Cancer Risk and Mutagenicity of Tea," Environmental Research 52: 23-33, 1990.

130. Rylander, R. and Koo, L.C., "Environmental Tobacco Smoke and Lung Cancer -- Recent Aspects on Confounders and Dose Levels." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 133-137, 1990.

131. Sterling, T., Weinkam, J. and Sterling, D., "Exposure of Homemakers to Toxic Contaminants: I. Differences in Chronic Conditions Between Homemakers and Employed Persons." In: Indoor Air '90: Proceedings of the 5th International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 471-476, July 29-August 3, 1990.

132. Holst, P.A., Kromhout, D. and Brand, R., "For Debate: Pet Birds as an Independent Risk Factor for Lung Cancer," British Medical Journal 297: 1319-1321, 1988.

2023468984

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

133. Repace, J. and Lowrey, A., "A Quantitative Estimate of Nonsmokers' Lung Cancer Risk from Passive Smoking," Environment International 11(1): 3-22, 1985.

134. Arundel, A., Irwin, T. and Sterling, T., "Nonsmoker Lung Cancer Risks from Tobacco Smoke Exposure: An Evaluation of Repace and Lowrey's Phenomenological Model," Journal of Environmental Science and Health C4(1): 93-118, 1986.

135. Anonymous, "The Murky Hazards of Secondhand Smoke," Consumer Reports: 81-84, February, 1985.

136. Arundel, A., Sterling, T. and Weinkam, J., "Never Smoker Lung Cancer Risks from Exposure to Particulate Tobacco Smoke," Environment International 13: 409-426, 1987.

137. Lebowitz, M.D., "The Potential Association of Lung Cancer with Passive Smoking," Environment International 12: 3-9, 1986.

138. Johnson, C. and Letzel, H., "Letter to the Editors," Environment International 12: 21-22, 1986.

139. Burch, P.R.J., "Health Risks of Passive Smoking: Problems of Interpretation," Environment International 12: 23-28, 1986.

140. Kilpatrick, S.J., "Letter to the Editors," Environment International 12: 29-31, 1986.

141. Repace, J. and Lowrey, A., "Risk Assessment Methodologies for Passive Smoking-Induced Lung Cancer," Risk Analysis 10(1): 27-38, 1990.

142. Darby, S. and Pike, M., "Lung Cancer and Passive Smoking: Predicted Effects from a Mathematical Model for Cigarette Smoking and Lung Cancer," British Journal of Cancer 58: 825-831, 1988.

143. Wald, N., Nanchahal, K., Cuckle, H. and Thompson, S., "Letter to the Editor: Lung Cancer and Passive Smoking," British Journal of Cancer 61: 337, 1990.

144. Darby, S.C. and Pike, M.C., "Response to the Letter from Dr. Wald," British Journal of Cancer 61: 337-338, 1990.

145. Uberla, K., "Epidemiology: Its Scope and Limitations for Indoor Air Quality." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 45-60, 1989.

2023468985

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

146. Miller, G.H., "Cancer, Passive Smoking and Nonemployed and Employed Wives," Western Journal of Medicine 140(4): 632-635, 1984.

147. Miller, G.H., "The Impact of Passive Smoking: Cancer Deaths Among Nonsmoking Women," Cancer Detection and Prevention 14(5): 497-503, 1990.

148. Arundel, A. and Sterling, T.D., "Review of the Epidemiological Studies on Lung Cancer and Nonsmoker's Exposure to Environmental Tobacco Smoke," Communication to the Special Projects Office, U.S. Office of Technology Assessment Health Program, Washington, D.C., April, 1986.

149. Sandler, D.P., Everson, R.B., Wilcox, A.J. and Browder, J.P., "Cancer Risk in Adulthood from Early Life Exposure to Parents' Smoking," American Journal of Public Health 75(5): 487-492, 1985.

150. Sandler, D.P., Wilcox, A.J. and Everson, R.B., "Cumulative Effects of Lifetime Passive Smoking on Cancer Risk," Lancet II: 312-314, 1985.

151. Sandler, D.P., Everson, R.B. and Wilcox, A.J., "Passive Smoking in Adulthood and Cancer Risk," American Journal of Epidemiology 121(1): 37-48, 1985.

152. Lee, P., "Lifetime Passive Smoking and Cancer Risk," Lancet II: 1444, 1985.

153. Burch, P., "Lifetime Passive Smoking and Cancer Risk," Lancet II: 866, 1985.

154. Burch, P., "Re: Passive Smoking in Adulthood and Cancer Risk," American Journal of Epidemiology 123(2): 368-369, 1986.

155. Higgins, I., "Lifetime Passive Smoking and Cancer Risk," Lancet II: 866-867, 1985.

156. Friedman, G., "Re: Passive Smoking in Adulthood and Cancer Risk," American Journal of Epidemiology 123(2): 367, 1986.

157. Mantel, N., "Re: Passive Smoking in Adulthood and Cancer Risk," American Journal of Epidemiology 123(2): 367-368, 1986.

158. Sandler, D.P., Comstock, G.W., Helsing, K.J. and Shore, D.L., "Deaths from All Causes in Non-Smokers Who Lived with Smokers," American Journal of Public Health 79(2): 163-167, 1989.

2023468986

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

159. Holcomb, L.C., "Risk to Passive Smokers," American Journal of Public Health 79(10): 1432, 1989.

160. Wells, A., "An Estimate of Adult Mortality in the United States from Passive Smoking," Environment International 14: 249-265, 1988.

161. Moghissi, A., "Cardiovascular Risks of Environmental Tobacco Smoke," Environment International 14: i, 1988.

162. Lee, P.N., "An Estimate of Adult Mortality in the United States from Passive Smoking: A Response," Environment International 16: 179-181, 1990.

163. Holcomb, L.C., "An Estimate of Adult Mortality in the United States from Passive Smoking: A Response," Environment International 16: 184-187, 1990.

164. Repace, J.L. and A.H. Lowrey, "Rebuttal to Lee/Katzenstein Commentary on Passive Smoking Risk," Environment International 16: 182-184, 1990.

165. Wells, A.J., "An Estimate of Adult Mortality in the United States from Passive Smoking: A Response to Criticism," Environment International 16: 187-193, 1990.

166. Vandenbroucke, J., Verheesen, J.H.H., de Bruin, A., Mauritz, B.J., van der Heide-Wessel, C. and van der Heide, R.M., "Active and Passive Smoking in Married Couples: Results of 25 Year Follow-Up," British Medical Journal I: 1801-1802, 1984.

167. Slattery, M.L., Robison, L.M., Schuman, K.L., French, T.K., Abbott, T.M., Overall, J.C. and Gardner, J.W., "Cigarette Smoking and Exposure to Passive Smoke Are Risk Factors for Cervical Cancer," Journal of the American Medical Association 261: 1593-1598, 1989.

168. Slattery, M.L., "Exposure to Cigarette Smoke and Cervical Cancer: In Reply," Journal of the American Medical Association 262(4): 499, 1989.

169. Zang, E.A., E.L. Wynder and R.E. Harris, "Exposure to Cigarette Smoke and Cervical Cancer," Journal of the American Medical Association 262(4): 499, 1989.

170. Kabat, G.C., Dieck, G.S. and Wynder, E.L., "Bladder Cancer in Nonsmokers," Cancer 57: 362-367, 1986.

171. Burch, J.D., Rohan, T.E., Howe, G.R., Risch, H.A., Hill, G.B., Steele, R. and Miller, A.B., "Risk of Bladder Cancer by Source

2023468987

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

and Type of Tobacco Exposure: A Case-Control Study," International Journal of Cancer 44: 622-628, 1989.

172. Grufferman, S., Wang, H.H., DeLong, E.R., Kimm, S.Y.S., Delzell, E.S. and Falletta, J.M., "Environmental Factors in the Etiology of Rhabdomyosarcoma in Childhood," Journal of the National Cancer Institute 68(1): 107-113, 1982.

173. John, E.M., Savitz, D.A. and Sandler, D.P., "Prenatal Exposure to Parents' Smoking and Childhood Cancer," American Journal of Epidemiology 133(2): 123-132, 1991.

174. Layard, M.W., "Environmental Tobacco Smoke and Cancer: The Epidemiologic Evidence." In: Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989. D. Ecobichon and J. Wu (eds.). Lexington, Massachusetts, Lexington Books, D.C. Heath and Co., 99-115, 1990.

2023468988

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Lung Function/Disease: Adults

The issue of a possible relationship between exposure to ETS and respiratory disease in nonsmokers was first raised in a 1980 study by two California researchers, White and Froeb.[1] On the basis of their measurements of the small airways function of smokers and nonsmokers in the workplace, they asserted that nonsmokers exposed to tobacco smoke at work for 20 or more years had reduced function of the small airways compared to nonsmokers who did not have such exposures. Other studies with similar findings have been reported since that time. In 1983, French researchers Kauffmann, et al., reported that nonsmoking spouses over 40 years of age who were married to smokers exhibited decreases in pulmonary function compared to nonsmoking spouses of nonsmokers.[2] A 1989 study by Hole, et al., of a Scottish population reported significantly lower pulmonary function among nonsmokers who lived with smokers compared to nonsmokers who were not exposed to ETS.[3]

However, each of these studies, particularly the White/Froeb study,[4-7] has been criticized for numerous reasons. In regard to the White/Froeb study, for example, a physician at a U.S. medical school questioned their use of carbon monoxide as an index of smoke exposure, contending that they "do not have reliable estimates of the smoke exposure in the environment of their nonsmokers" because it is not unique to tobacco smoke.[7] A British

2023468989

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

reviewer shared the physician's view that their findings "relate to an index which is contentious and certainly not an accepted reliable indicator of an increased health risk."[8] White and Froeb themselves noted that the average values of the pulmonary tests of nonsmokers exposed to tobacco smoke "were not notably different" from the values suggested as normal by a specialist in this area.[9]

Perhaps the most telling criticisms of the study were voiced by Dr. Michael Lebowitz of the University of Arizona at an annual joint meeting of the American Lung Association/American Thoracic Society and in a subsequent letter published in the U.S. Congressional Record.[10-11] During a forum at the ALA meeting, Dr. Lebowitz stated that he had concluded, from his own extensive review of the study and from an interview with White, that the study was "improperly designed" from an epidemiological point of view. He noted that there were problems "inherent" in the study, including the selection of the study group and the measurement of smoke in the workplace. Dr. Lebowitz also expressed concern that the statistical significance of the data appeared to depend on the unexplained omission of data for 3,000 people who were originally included in the study. Based upon these considerations, Dr. Lebowitz urged that the study not be used to support the claim that ETS affects the lung function of adults in the workplace.

2023468990

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Dr. Lebowitz again took issue with the White/Froeb study in 1984 in a paper he presented at the Vienna Symposium on Passive Smoking. He contended:

> Even with a biased population, poor study design, and incorrect statistical evaluation, there were no clear-cut, consistent, medically meaningful differences between passive smokers and groups of nonsmokers; a corrected statistical analysis strengthened this conclusion.[12]

In the same paper, Dr. Lebowitz also questioned the findings of the 1983 French study which reportedly found significant differences in lung function between exposed and nonexposed nonsmokers in one part of the study population but no significant differences in the population as a whole. Dr. Lebowitz noted that since the "healthiest" part of the study population lived in the most polluted areas, the study may have been flawed due to biased population selection and testing or other confounding factors.[12]

In addition to these concerns, the results of the White/Froeb, the French and the Scottish studies appear to be inconsistent with other research on lung disease and lung function in nonsmokers. For example, a 1984 study of 1,351 German office workers by Kentner, et al., reportedly found no effect of ETS on pulmonary function among exposed nonsmokers.[13] In a 1988 update

2023468991

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

of the study, the investigators noted that "there is no evidence that average everyday passive smoke exposure in the office or at home leads to an essential reduction of lung function in healthy adults."[14] The key investigator for the study reported these same findings in 1989 and 1990 publications.[15,16]

Similarly, Canadian researchers Shephard, et al., reported that their analysis of a group of healthy young adult nonsmokers showed "no consistent reaction" of static lung volumes and insignificant changes of other lung function measurements when they were exposed to tobacco smoke.[17]

Numerous studies of individuals exposed to ETS in the home also present conclusions which appear to be contrary to these three studies. In 1981, Comstock, et al., epidemiologists at the Johns Hopkins University School of Medicine in New York, reported that in a group of 1,724 adults, the frequency of respiratory symptoms in nonsmokers was <u>not</u> significantly associated with the number of smokers in the household.[18] Nor was the frequency of impaired ventilatory function significantly higher if there were smokers in the home. However, their analysis did show that "among men who never smoked cigarettes, gas cooking was definitely associated with impaired ventilatory function, even when corrected for multiple comparisons."

2023468992

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Other studies on pulmonary function, respiratory disease and environmental tobacco smoke deserve special mention. In 1983, for example, Jones, et al., reported that in a case-control study of several hundred nonsmoking women from a U.S. study population, there was no significant association between decreases in lung function and exposure to ETS in the home.[19] Similarly, Lebowitz, et al., coordinators of an epidemiologic study of obstructive lung disease in Arizona, reported finding no effects from ETS exposures in the home in their adult study population.[20] In a study of 376 families, Yale University scientists Schilling, et al., also reportedly found no evidence that environmental tobacco smoke affects either lung function or respiratory symptoms in adults.[21]

More recently, in a Canadian study on the effect of indoor and outdoor pollutants on the lung function of housewives, Hosein and Corey concluded that ETS exposure did not significantly influence lung function, but that gas stove usage played a role in average lung function decline.[22] These findings have been reported by others. For example, a Japanese research group, Nitta, et al., has also reported that gas stove usage affects the respiratory health of adults.[23] Koo and Ho recently studied the effects of indoor nitrogen dioxide (NO_2) levels on respiratory illness rates in Hong Kong.[24] They reported that indoor NO_2 levels were associated with allergic rhinitis and chronic bronchitis in non-

2023468993

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

smoking mothers, but that there was no relationship between environmental tobacco smoke and NO_2 levels in the home environment.

In 1990, a Greek research group, Kalandidi, et al., investigated the possible relationship between reported tobacco smoke exposure and chronic obstructive pulmonary disease (COPD) in adult nonsmokers.[25] Although they reported finding increased risks of COPD among nonsmokers reportedly exposed to ETS, it is not clear whether they adequately considered other potential exposures which have been associated with the development of COPD such as occupation and outdoor air pollution. Another study published in 1990 by Lebowitz and Quackenboss reported that while they observed an increase in several acute respiratory symptoms associated with exposure to ETS, they noted "no relationship between the prevalence rates for chronic symptoms and diseases and the presence or amount of ETS in the home."[26]

In 1990, Jedrychowski, et al., reported an increased occurrence of respiratory illness among a group of elderly women exposed to ETS, but conceded that the reported effects were "greatly confounded by other indoor pollutants, especially those associated with cooking the meals on gas ovens." They also conceded that they considered only "the current passive smoking experience at home and took no account of the history of passive smoking that

2023468994

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

might have been present in the work place," which could "evidently bias the results of the study with respect to passive smoking."[27]

Researchers who have analyzed these reported findings contend that the results are mixed and inconclusive. For example, researchers in France, Laurent, et al., have commented that purported long-term health effects from exposure to ETS are difficult to demonstrate in healthy adults and that the results of the epidemiological studies are "sometimes conflicting and often open to question."[28] One investigator who is critical of ETS conceded that "the effect of passive smoking on respiratory infections in adults has not been well characterized and reports of its effects on chronic respiratory disease in adults have been inconsistent."[29]

In his summary of the studies of respiratory symptoms and disease in adults published up to early 1990, American investigator Dr. Philip Witorsch noted that "4 of 8 [reported] an increased frequency, 4 of 8 no increased frequency."[30] He stated that, in addition to "all of the problems" with the studies, "these results are too variable to permit any conclusion of association." As his summary demonstrates, the conclusion of the participants at the 1983 U.S. National Institutes of Health workshop on ETS exposure, that the possible effect from ETS "varies from negligible to quite small,"[31] is still pertinent.

2023468995

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Lung Function/Disease: Adults

1. White, J.R. and Froeb, H.F., "Small-Airways Dysfunction in Nonsmokers Chronically Exposed to Tobacco Smoke," The New England Journal of Medicine 302 (13): 720-723, 1980.

2. Kauffmann, F., Tessier, J.F. and Oriol, P., "Adult Passive Smoking in the Home Environment: A Risk Factor for Chronic Airflow Limitation," American Journal of Epidemiology 117(3): 269-280, 1983.

3. Hole, D.J., Gillis, C.R., Chopra, C. and Hawthorne, V.M., "Passive Smoking and Cardiorespiratory Health in a General Population in the West of Scotland," BMJ 299: 423-427, 1989.

4. Adlkofer, F., Scherer, G. and Weimann, H., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 392, 1980.

5. Huber, G., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 392, 1980.

6. Freedman, A., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393, 1980.

7. Aviado, D., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393, 1980.

8. Lee, P.N., "Passive Smoking," Food Chemistry and Toxicology 20: 223-229, 1982.

9. White, J. and Froeb, H., "Small-Airways Dysfunction in Passive Smokers," New England Journal of Medicine 303(7): 393-394, 1980.

10. Lebowitz, M., "Forum: Second Hand Smoke -- How Dangerous?," Presentation to the American Lung Association/American Thoracic Society Annual Meeting, Los Angeles, California, May 17, 1982.

11. Fountain, L.H., Statement, Re: "White-Froeb Study Discredited by Scientists." In: U.S. Congressional Record, 97th Congress, 2nd Session, E5252-5254, December 16, 1982.

12. Lebowitz, M., "Influence of Passive Smoking on Pulmonary Function: A Survey," Preventive Medicine 13(6): 645-655, 1984.

2023468996

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

13. Kentner, M., Triebig, G. and Weltle, D., "The Influence of Passive Smoking on Pulmonary Function - A Study of 1,351 Office Workers," Preventive Medicine 13(6): 656-669, 1984.

14. Kentner, M. and Weltle, D., "Passive Tobacco Smoke Inhalation and Lung Function in Adults." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 232-241, 1988.

15. Kentner, M., Weltle, D. and Valentin, H., "Passive Smoking and Lung Function in Adults," Arbeitsmedicine Sozialmedicine Praventivmedicine (24): 8-13, 1989.

16. Kentner, M. and Weltle, D., "Are There Any Impairments of Maximal Expiratory Flow-Volume Curves by Passive Smoking?" In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 153-166, 1990.

17. Shephard, R.J., Collins, R. and Silverman, F., "Responses of Exercising Subjects to Acute 'Passive' Cigarette Smoke Exposure," Environmental Research 19(1): 279-291, 1979.

18. Comstock, G.W., Meyer, M.B., Helsing, K.J. and Tockman, M.S., "Respiratory Effects of Household Exposures to Tobacco Smoke and Gas Cooking," American Review of Respiratory Disease 124(2): 143-148, 1981.

19. Jones, J.R., Higgins, I.T.T., Higgins, M.W. and Keller, J.B., "Effects of Cooking Fuels on Lung Function in Nonsmoking Women," Archives of Environmental Health 38(4): 219-222, 1983.

20. Lebowitz, M.D., Knudson, R.J. and Burrows, B., "Family Aggregation of Pulmonary Function Measurements," American Review of Respiratory Disease 129: 8-11, 1984.

21. Schilling, R.S.F., Letai, A.D., Hui, S.L., Beck, G.J., Schoenberg, J.B. and Bouhuys, A., "Lung Function, Respiratory Disease, and Smoking in Families," American Journal of Epidemiology 106(4): 274-283, 1977.

22. Hosein, H.R. and Corey, P., "Domestic Air Pollution and Respiratory Function in a Group of Housewives," Canadian Journal of Public Health 77: 44-50, 1986.

23. Nitta, H., Nakai, S. and Maeda, K., "Indoor Nitrogen Dioxide Pollution Associated with Gas Stoves and Unvented Heaters in Japan." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 364-370, 1990.

2023468997

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

24. Koo, L.C. and Ho, J.H.C., "Sources of Nitrogen Dioxide in Homes and Its Association with Respiratory Illness in Hong Kong." In: Indoor Air Quality and Ventilation. London, Selper, Ltd, 287-294, 1990.

25. Kalandidi, A., Trichopoulos, D., Hatzakis, A., Tzannes, S. and Saracci, R., "The Effect of Involuntary Smoking on the Occurrence of Chronic Obstructive Pulmonary Disease," Soz Praeventivmed 35: 12-16, 1990.

26. Lebowitz, M.D. and Quackenboss, J.J., "The Effects of Environmental Tobacco Smoke on Pulmonary Function." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 147-151, 1990.

27. Jedrychowski, W., Tobiasz-Adamczyk, B., Mroz, E. and Cecek, J. "Chest Diseases of Elderly Women Due to Domestic Cooking and Passive Smoking: The Cracow Study." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 249-255, 1990.

28. Laurent, A.M., Courtois, Y.A., Pretet, S. and Claude, J.R., "Evaluation of Exposure to Ambient Tobacco Smoke: A Few Concrete Examples Concerning the Value of Biological Atmospheric Indicators." In: Present and Future of Indoor Air Quality. C.J. Bieva, Y. Courtois, M. Govaerts (eds.). Amsterdam, Excerpta Medica, 103-110, 1989.

29. Graham, N.M.H., "The Epidemiology of Acute Respiratory Infections in Children and Adults: A Global Perspective," Epidemiologic Reviews 12: 149-178, 1990.

30. Witorsch, P., "Health Effects of Environmental Tobacco Smoke." In: Toxicology Forum: 1990 Annual Winter Meeting. Washington D.C., 212, February 19-21, 1990.

31. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies, May 1-3, 1983, December, 1983.

2023468998

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

"Compromised Individuals": Adults

Asthmatics are believed to be particularly vulnerable to various environmental influences, including ETS, but the scientific data in this area are contradictory and inconclusive. A 1981 study by Dahms, et al., for example, reported decreases in the pulmonary function of several asthmatics exposed to environmental tobacco smoke.[1] However, the study suffers from several obvious limitations, including the unrealistic conditions under which the subjects were exposed to ETS; they were challenged with high levels of smoke in an enclosed smog chamber. In addition, as the authors themselves noted, their experiment lacked proper controls and the effects observed may have been due to psychological, not physical, factors.

Contrary to Dahms, et al., a Canadian group, Pimm, et al., observed no systematic lung changes among asthmatics exposed to levels of tobacco smoke typically found in public places.[2] Later research by the co-authors of this study supports this conclusion. They reported that respiratory data collected from a group of asthmatic volunteers exposed to tobacco smoke "do not suggest that asthmatic subjects have an unusual sensitivity" to such exposure.[3] Although several volunteers claimed to have experienced wheezing and tightness in the chest due to the exposure, the researchers determined that the "physiological data give little

2023468999

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

support to the concept of a subgroup with particular sensitivity." They noted that these reactions probably were due to the "suggestibility" of the subjects.

The difficulty in determining the impact of psychological responses in such studies is clearly demonstrated by the results of two reports from Australia. Although a 1985 report by Knight and Breslin suggests that short-term ETS exposures are capable of inducing reactions in asthmatics,[4] an earlier study co-authored by Breslin tends to support the theory that psychological reactions may partially explain symptoms observed during such exposures. In that study, Breslin and Ing reported that although asthmatics exposed to tobacco smoke complained of subjective symptoms, no significant objective evidence of airways obstruction was observed.[5]

Other studies also fail to provide support for claims regarding a relationship between ETS exposure and reactions in asthmatics. For example, Wiedemann, et al., at Yale University, examined the short-term effects of ETS exposure on a group of young asthmatic patients and observed no changes in lung flow rates.[6] They concluded that such exposures present "no acute respiratory risk" to asthmatics.

Tulane University scientists Stankus, et al., recently assessed the effects of heavy exposure to ETS in a group of self-

2023469000

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

reported "tobacco smoke-sensitive" asthmatics. They reported that two-thirds of the subjects did not experience significant changes in pulmonary function even after heavy, prolonged exposure to ETS, and that there was no association between reactions to ETS and hypersensitivity to tobacco leaf extract, which is commonly used in allergy testing.[7]

A report by Lebowitz on data from a large-scale epidemiological study in the U.S. suggests that ETS in the home does not affect symptoms or pulmonary function in either children or adult asthmatics, but that dust and pollen in the home apparently can provoke such effects.[8] Another group of U.S. researchers, Bailey, et al., also recently reported that exposure to ETS did not impair lung function in 263 asthmatic adult subjects.[9]

2023469001

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

"Compromised Individuals": Adults

1. Dahms, T.E., Bolin, J.F. and Slavin, R.G., "Passive Smoking Effects on Bronchial Asthma," Chest 80(5): 530-534, 1981.

2. Pimm, P.E., Shephard, R.J. and Silverman, F., "Physiological Effects of Acute Passive Exposure to Cigarette Smoke in Asthmatics," Federal Proceedings 36(3): 606, 1977. Abstract.

3. Shephard, R.J., Collins, R. and Silverman, F., "'Passive' Exposure of Asthmatic Subjects to Cigarette Smoke," Environmental Research 20: 392-402, 1979.

4. Knight, A. and Breslin, A.B.X., "Passive Cigarette Smoking and Patients with Asthma," The Medical Journal of Australia 142: 194-195, 1985.

5. Ing, A. and Breslin, A.B.X., "The Effect of Passive Cigarette Smoking on Asthmatic Patients," Proceedings, The Thoracic Society of Australia, 543, October, 1983. Abstract.

6. Wiedemann, H.P., Mahler, D.A., Loke, J., Virgulto, J.A., Snyder, P. and Matthay, R.A., "Acute Effects of Passive Smoking on Lung Function and Airway Reactivity in Asthmatic Subjects," Chest 89(2): 180-184, 1986.

7. Stankus, R.P., Menon, P.K., Rando, R.J., Glindmeyer, H., Salvaggio, J.E. and Lehrer, S.B., "Cigarette Smoke-Sensitive Asthma: Challenge Studies," Journal of Allergy and Clinical Immunology 82: 331-338, 1988.

8. Lebowitz, M., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families." In: ETS-Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson, M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 90-97, 1984.

9. Bailey, W.C., Richards, J.M., Manzella, B.A., Brooks, C.M., Windsor, R.A. and Soong, S.J., "Characteristics and Correlates of Asthma in a University Clinic Population," Chest 98(4): 821-828, 1990.

2023469002

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Lung Function/Disease: Children

Perhaps no claim regarding ETS is as capable of provoking strong feelings as the charge that parents who smoke may harm the health of their children. While the issue of parental smoking is laden with emotion, the scientific basis for the claim is difficult to interpret. For example, while one study examines respiratory symptoms or illness such as coughs and colds by questionnaire responses from parents,[1] another measures lung function with special equipment at a school or health facility.[2] In the U.S. alone, according to one report, this has led to a situation in which studies of ETS and the respiratory system are "being carried out by at least three different groups, are employing different populations and methodologies and have led to varying conclusions."[3]

Perhaps not surprisingly, such studies, each with a different sample size, data collection method, and analysis, tend to yield factually incompatible and contrary conclusions. For instance, although certain studies have reported adverse findings between parental smoking and respiratory illness in children,[4-35] others have observed no significant relationship.[1,36-51] After a five-year study of over 400 children, for example, a Dutch research group concluded there was "no evidence" that parental smoking had an appreciable effect on respiratory symptoms in school children.[43]

2023469003

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

A similar conclusion was reached by a group of U.S. researchers, including a critic of smoking, who found "no significant relation" between parental smoking and respiratory symptoms in a study of nearly 400 families with 816 children in three cities.[36]

The contradictory nature of findings on the issue of parental smoking is also apparent in the growing number of studies examining the relationship between parental smoking and children's respiratory or lung function. Although several reports have claimed that parental smoking results in decreased pulmonary function in children,[8,13-14,32,52-60] others have not,[61-64] including those of a U.S. research group who have published a series of studies on this subject.[2,65-67] In 1982, for example, the U.S. group showed that a comparison of body size with lung function eliminated any reported correlation between parental smoking and children's lung function.[2] Two years later, a reanalysis of data from families in their study population again showed that "parental smoking did not have a significant effect on children's pulmonary function; smoking habits of others in the household (predominantly siblings) did not have any effect either."[66]

Moreover, the authors of studies reporting adverse effects from ETS exposures among children concede that their conclusions must be viewed with caution because of numerous confounding factors. The potential impact of such factors was given special consideration

2023469004

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

in the report from a workshop on ETS sponsored by the U.S. National Institutes of Health.[3] After listing numerous such factors, including types of heating used, socio-economic status and demographic and medical characteristics of the study population, the report cautioned "that any study which ignores them will be seriously flawed."

The importance of such factors in evaluating the outcome of research on parental smoking is supported by a number of reports which have shown that the use of gas stoves in the home may be independently associated with respiratory disease[40,65,68-72] and impaired pulmonary performance[73-74] in children. One group of British researchers acknowledged the possible influence of factors such as cross-infection in the home and genetic susceptibility to childhood respiratory illness and symptoms.[11-12] More recently, researchers in Hong Kong reported "a highly significant correlation" between the frequency of respiratory illnesses of mothers and their children.[75]

Other confounding factors independent of parental smoking have been reported recently in the literature. For example, studies in the United Kingdom have identified damp housing[46, 76-79] and paternal occupation[80] as potential explanatory factors for the occurrence of respiratory illness in children. Other recent studies have identified outdoor air pollution,[82-85] infections

2023469005

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

transmitted during day-care attendance[49,86-87], decreased breast-feeding[88] and the use of kerosene heaters and woodburning stoves in the home[89-91] as factors related to childhood respiratory disease.

The relevance of dampness in the etiology of respiratory symptoms in children is supported by current research which links dampness with the presence of molds, dust mites, fungi and other allergenic microbes. The growth of fungi and molds in the home is directly related to respiratory symptoms and sensitization reactions in some individuals.[78,92-94] Recent investigations report, moreover, that exposure to ETS does not increase sensitization to common allergens in children.[95-96]

Others have conceded that the reliance of such studies on questionnaires for information about respiratory symptoms casts doubt on their reported findings. In one study that reported a significant association between parental smoking and respiratory symptoms, for example, it was noted that even "slight changes" in the way the questions were phrased could result "in substantial differences in the type of responses one obtains."[14] Similarly, another study observed that there was a significant difference in the respiratory symptoms reported depending on which parent completed the questionnaire.[24] Authors of another study that reported adverse effects of parental smoking on the respiratory

2023469006

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

health of children conceded that "since the exposure variables used in these analyses were subject to substantial measurement error, a more refined measurement of personal exposure is required."[29] One researcher who is critical of parental smoking has stated that "quantitative assessment of involuntary exposure of infants and children to ETS has been very imprecise and probably inaccurate."[97]

Studies utilizing seemingly more objective standards such as actual measurements of lung function are also open to criticism. Even reviewers of the literature who are critical of parental smoking concede that the tests used in these studies are "influenced by a large number of variables."[98] They list age, height, and gender of the test subject as well as his or her motivation, cooperation, and effort put forth during the test, the skill and experience of the operator, and the type of instrumentation used as variables that can affect the results of pulmonary function measurements. The reviewers explain that these problems are especially important in pulmonary function measures taken in children. In 1989, two American co-researchers, Witorsch and Witorsch, reported that "it has been shown that mean pulmonary performance within a single group of children can vary significantly from one spirometry test to the next without any apparent cause" and that it "is noteworthy that such statistically significant

2023469007

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

differences are similar in magnitude to most of the small decrements in pulmonary function reported in children of smoking parents."[99]

The shortcomings of studies analyzing the relationship between ETS exposure and childhood health were highlighted in a 1988 report by two U.S. investigators who re-examined 30 such studies and evaluated them for their scientific validity.[100] They noted that while several studies of adequate scientific design had reported a statistically significant relationship between ETS exposures and childhood health, "most studies had significant design problems that prevent reliance on their conclusions." The authors concluded that "many questions remain, and future studies should consider important methodological standards to determine more accurately the effect of passive smoking on child health."

Thus, claims that parental smoking plays a causal role in the development of respiratory symptoms and reduced lung function in children are not scientifically justified. Such claims are typically based upon a single study of a selected symptom (such as cough or wheeze). These kinds of studies invariably fail to consider nutrition, health habits of the family, and other lifestyle variables. Similarly, studies that report reduced lung function in children of smoking parents fail to address the issue of socio-economic status or the potential role of genetic and family traits in pulmonary function capabilities.[64] Moreover, the reductions

2023469008

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

reported in the literature are small and of uncertain clinical or biological significance, and are contradicted by a number of studies that reportedly have observed no effect of parental smoking on children's lung function.

2023469009

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Lung Function/Disease: Children

1. Camacho, E., Colomer, P.R. and Betoret, J.L.D., "Pulmonary Symptoms and Pulmonary Functional Tests Among Children in Relation to the Area of Residence," European Respiratory Diseases 63(2): 165-166, 1982.

2. Lebowitz, M., Armet, D.B. and Knudson, R., "The Effect of Passive Smoking on Pulmonary Function in Children," Environment International 8: 371-373, 1982.

3. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Report of Workshop on Respiratory Effects of Involuntary Smoke Exposure: Epidemiologic Studies, May 1-3, 1983, December, 1983.

4. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

5. U.S. Department of Health and Human Services, Public Health Services, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

6. Bland, M., Bewley, B.R., Pollard, V. and Banks, M.H., "Effect of Children's and Parents' Smoking on Respiratory Symptoms," Archives of Diseases in Childhood 53(2): 100-105, 1978.

7. Bonham, G. and Wilson, R., "Children's Health in Families With Cigarette Smokers," American Journal of Public Health 71(3): 290-293, 1981.

8. Burchfiel, C., Higgins, M.W., Keller, J.B., Howatt, W.F., Butler, W.J. and Higgins, I.T.T., "Passive Smoking in Childhood: Respiratory Conditions and Pulmonary Function in Tecumseh, Michigan," American Review of Respiratory Disease 133(6): 966-973, 1986.

9. Cameron, P. and Robertson, D., "Effect of Home Environment Tobacco Smoke on Family Health," Journal of Applied Psychology 57(2): 142-147, 1973.

10. Chen, Y., "Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood," Chest 95: 1004-1007, 1989.

2023469010

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

11. Colley, J., "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production," British Medical Journal II: 201-204, 1974.

12. Colley, J., Holland, W.W. and Corkhill, R.T., "Influence of Passive Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early Childhood," Lancet II: 1031-1034, 1974.

13. Dockery, D., Speizer, F.E., Stram, D.O., Ware, J.H., Spengler, J.D. and Ferris, B.G., "Effects of Inhalable Particles on Respiratory Health of Children," American Review of Respiratory Disease 139: 587-594, 1989.

14. Ekwo, E., Weinberger, M.M., Lachenbruch, P.A. and Huntley, W.H., "Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children," Chest 84(6): 662-668, 1983.

15. Fergusson, D., Horwood, L.J., Shannon, F.T. and Taylor, B., "Parental Smoking and Lower Respiratory Illness in the First Three Years of Life," Journal of Epidemiology and Community Health 35(3): 180-184, 1981.

16. Fergusson, D. and Horwood, L.J., "Parental Smoking and Respiratory Illness During Early Childhood: A Six-year Longitudinal Study," Pediatric Pulmonology 1(2): 99-106, 1985.

17. Ferris, B., Dockery, D.W., Ware, J.H., Speizer, F.E. and Spiro, R., "The Six-City Study: Examples of Problems in Analysis of Data," Environmental Health Perspectives 52: 115-123, 1983.

18. Gortmaker, S., Walker, D.K., Jacobs, F.H. and Ruch-Ross, H., "Parental Smoking and the Risk of Childhood Asthma," American Journal of Public Health 72(6): 574-579, 1982.

19. Harlap, S. and Davies, A., "Infant Admissions to Hospital and Maternal Smoking," Lancet I: 529-532, 1974.

20. Kraemer, M., Richardson, M.A., Weiss, N.S., Furukawa, C.T., Shapiro, G.G., Pierson, W.E. and Bierman, C.W., "Risk Factors for Persistent Middle Ear Effusions: Otitis Media, Catarrh, Cigarette Smoke Exposure, and Atopy," Journal of the American Medical Association 249(8): 1022-1025, 1983.

21. Murray, A. and Morrison, B., "Passive Smoking and the Seasonal Difference of Severity of Asthma in Children," Chest 94(4): 701-708, 1988.

2023469011

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

22. Neuspiel, D., Rush, D., Butler, N.R., Golding, J., Bijur, P.E. and Kurzon, M., "Parental Smoking and Post-Infancy Wheezing in Children: A Prospective Cohort Study," American Journal of Public Health 79(2): 168-171, 1989.

23. Ogston, S., Florey, C.D.V. and Walker, C.H.M., "Association of Infant Alimentary and Respiratory Illness with Parental Smoking and Other Environmental Factors," Journal of Epidemiology and Community Health 41(1): 21-25, 1987.

24. Schenker, M., Samet, J.M. and Speizer, F.E., "Risk Factors for Childhood Respiratory Disease: The Effect of Host Factors and Home Environmental Exposures," American Review of Respiratory Disease 128: 1038-1043, 1983.

25. Somerville, S., Rona, R.J. and Chinn, S., "Passive Smoking and Respiratory Conditions in Primary School Children," Journal of Epidemiology and Community Health 42(2): 105-110, 1988.

26. Strachan, D., Jarvis, M.J. and Feyerabend, C., "Passive Smoking, Salivary Cotinine Concentrations, and Middle Ear Effusion in 7 Year Old Children," British Medical Journal 298: 1549-1552, 1989.

27. Tsimoyianis, G., Jacobson, M.S., Feldman, J.G., Antonio-Santiago, M.T., Clutario, B.C., Nussbaum, M. and Schenker, I.R., "Reduction in Pulmonary Function and Increased Frequency of Cough Associated With Passive Smoking in Teenage Athletes," Pediatrics 80(1): 32-36, 1987.

28. Ware, J., Dockery, D.W., Spiro, A., Speizer, F.E. and Ferris, B.G., "Passive Smoking, Gas Cooking, and Respiratory Health of Children Living in Six Cities," American Review of Respiratory Disease 129: 366-374, 1984.

29. Ugnat, A.M., Mao, Y., Miller, A.B. and Wigle, D.T., "Effects of Residential Exposure to Environmental Tobacco Smoke on Canadian Children," Canadian Journal of Public Health 81(5): 345-349, 1990.

30. Greenberg, R.A., Bauman, K.E., Glover, L.H., Strecher, V.J., Kleinbaum, D.G., Haley, N.J., Stedman, H.C., Fowler, M.G. and Loda, F.A., "Ecology of Passive Smoking by Young Infants," Journal of Pediatrics 114: 774-780, 1989.

31. Berg, A.T., Shapiro, E.D. and Capobianco, L.A., "Group Day Care and the Risk of Serious Infectious Illnesses," American Journal of Epidemiology 133(2): 154-163, 1991.

2023469012

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

32. Dijkstra, L., Houthuijs, D., Brunekreef, B., Akkerman, I. and Boleij, J.S.M., "Respiratory Health Effects of the Indoor Environment in a Population of Dutch Children," American Review of Respiratory Disease 142: 1172-1178, 1990.

33. McConnochie, K.M. and Roghmann, K.J., "Wheezing at 8 and 13 Years: Changing Importance of Bronchiolitis and Passive Smoking," Pediatric Pulmonology 6(3): 138-146, 1989.

34. Woodward, A., Douglas, R.M., Graham, N.M. and Miles, H., "Acute Respiratory Illness in Adelaide Children: Breast Feeding Modifies the Effect of Passive Smoking," Journal of Epidemiology and Community Health 44: 224-230, 1990.

35. Stern, B., Raizenne, M. and Burnett, R., "Respiratory Effects of Early Childhood Exposure To Passive Smoke," Environment International 15: 29-34, 1989.

36. Schilling, R., Letai, A.D., Hui, S.L., Beck, G.J., Schoenberg, J.B. and Bouhuys, A., "Lung Function, Respiratory Disease, and Smoking in Families," American Journal of Epidemiology 106(4): 274-283, 1977.

37. Binder, R., Mitchell, C.A., Hosein, H.R. and Bouhuys, A., "Importance of the Indoor Environment in Air Pollution Exposure," Archives of Environmental Health 31(6): 277-279, 1976.

38. Bouhuys, A., Lung Diseases in Rural and Urban Communities, Report Number HR-42912-1F, Sponsored by the Division of Lung Diseases, National Heart, Lung and Blood Institute, U.S. National Institutes of Health, Bethesda, Maryland, 77-89, June 10, 1977.

39. Gardner, G., Frank, A.L. and Taber, L.H., "Effects of Social and Family Factors on Viral Respiratory Infection and Illness in the First Year of Life," Journal of Epidemiology and Community Health 38: 42-48, 1984.

40. Harrington, W. and Krupnick, A., "Short-Term Nitrogen Dioxide Exposure and Acute Respiratory Disease in Children," Journal of the Air Pollution Control Association 35: 1061-1067, 1985.

41. Holma, B. and Winding, O., "Housing, Hygiene, and Health: A Study in Old Residential Areas in Copenhagen," Archives of Environmental Health 32(2): 86-93, 1977.

42. Kallail, K., Rainbolt, H.R. and Bruntzel, M.D., "Passive Smoking and Middle Ear Problems in Kansas Public School

2023469013

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Children," Journal of Communicable Disorders 20: 187-196, 1987.

43. Kerrebijn, J., Hoogeveen-Schroot, H.C.A. and van der Wal, M.C., "Chronic Nonspecific Respiratory Disease in Children, A Five Year Follow-Up Study," Acta Paediatr Scand Suppl. 261: 11-72, 1977.

44. Lebowitz, M. and Burrows, B., "Respiratory Symptoms Related to Smoking Habits of Family Adults," Chest 69(1): 48-50, 1976.

45. Love, G., Lan, S.P., Shy, C.M. and Struba, R.J., "The Incidence and Severity of Acute Respiratory Illness in Families Exposed to Different Levels of Air Pollution, New York Metropolitan Area, 1971-72," Archives of Environmental Health 36(2): 66-73, 1981.

46. Martin, C., Platt, S.D. and Hunt, S.M., "Housing Conditions and Ill Health," British Medical Journal 294: 1125-1127, 1987.

47. Salzman, M., Biller, H.F. and Schechter, C.B., "Passive Smoking and Croup," Archives of Otolaryngology and Head Neck Surgery 113: 866-868, 1987.

48. Shy, C., Creason, J.P., Pearlman, M.E., McClain, K.E., Benson, F.B. and Young, M.M., "The Chattanooga School Children Study: Effects of Community Exposure to Nitrogen Dioxide. II. Incidence of Acute Respiratory Illness," Journal of the Air Pollution Control Association 20(9): 582-588, 1970.

49. Harsten, G., Prellner, K., Heldrup, J., Kalm, O. and Kornfalt, R., "Acute Respiratory Tract Infections in Children: A Three-Year Follow-up from Birth," Acta Paediatr Scand 79(4): 402-409, 1990.

50. Thorton, A.J., Morley, C.J., Hewson, P.H., Cole, T.J., Fowler, M.A. and Tunnacliffe, J.M., "Symptoms in 298 Infants Under 6 Months Old, Seen at Home," Archives of Disease in Childhood 65(3): 280-285, 1990.

51. Victora, C.G., Smith, P.G., Barros, F.C., Vaughan, J.P. and Fuchs, S.C., "Risk Factors for Deaths Due to Respiratory Infections Among Brazilian Infants," International Journal of Epidemiology 18(4): 918-925, 1989.

52. Berkey, C., Ware, J.H., Dockery, D.W., Ferris, B.G. and Speizer, F.E., "Indoor Air Pollution and Pulmonary Function Growth in Preadolescent Children," American Journal of Epidemiology 123(2): 250-260, 1986.

2023469014

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

53. Chen, Y. and Li, W., "The Effect of Passive Smoking on Children's Pulmonary Function in Shanghai," American Journal of Public Health 76(5): 515-518, 1986.

54. Corbo, G., Foresi, A., Valente, S. and Bustacchini, S., "Maternal Smoking and Bronchial Responsiveness in Children," American Review of Respiratory Disease 137(1): 245, 1987.

55. Hasselblad, V., Humble, C.G., Graham, M.G. and Anderson, H.S., "Indoor Environmental Determinants of Lung Function in Children," American Review of Respiratory Disease 123(5): 479-485, 1981.

56. Kauffmann, F., Tager, I.B., Munoz, A. and Speizer, F.E., "Familial Factors Related to Lung Function in Children Aged 6-10 Years," American Journal of Epidemiology 129(6): 1289-1299, 1989.

57. Masi, M., Hanley, J.A., Ernst, P. and Becklake, M.R., "Environmental Exposure to Tobacco Smoke and Lung Function in Young Adults," American Review of Respiratory Disease 138: 296-299, 1988.

58. Tager, I., Munoz, A., Rosner, B., Weiss, S.T., Carey, V. and Speizer, F.E., "Effect of Cigarette Smoking on the Pulmonary Function of Children and Adolescents," American Review of Respiratory Disease 131(5): 752-759, 1985.

59. Tager, I., Weiss, S.T., Munoz, A., Rosner, B. and Speizer, F.E., "Longitudinal Study of the Effects of Maternal Smoking on Pulmonary Function in Children," New England Journal of Medicine 309(120): 699-703, 1983.

60. Tashkin, D., Clark, V.A., Simmons, M., Reems, C., Coulson, A.H., Bourque, L.B., Sayre, J.W., Detels, R. and Rokaw, S., "The UCLA Population Studies of Chronic Obstructive Respiratory Disease. VII. Relationship Between Parental Smoking and Children's Lung Function," American Review of Respiratory Disease 129: 891-897, 1984.

61. Dodge, R., "The Effects of Indoor Pollution on Arizona Children," Archives of Environmental Health 37(3): 151-155, 1982.

62. Hosein, R. and Corey, P., "Multivariate Analysis of Nine Indoor Factors on FEV_1 of Caucasian Children," American Thoracic Society Meeting, Miami Beach, Florida, May 20-23, 1984. Poster Session #32.

2023469015

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

63. Mandi, A., Galambos, E., Galgoczy, G., Szabo, M. and Kollar, K., "Relationship Between Lung Function Values and Air Pollution Data in Budapest School Children," Pneumonologie 150(2/4): 217-225, 1974.

64. Witorsch, R. and Witorsch, P., "Maternal Smoking and Pulmonary Performance in Children: A Critical Analysis," Indoor Air '87, Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Berlin, 175-179, August 17-21, 1987.

65. Lebowitz, M., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families." In: ETS-Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 90-97, 1984.

66. Lebowitz, M., Knudson, R.J. and Burrows, B., "Family Aggregation of Pulmonary Function Measurements," American Review of Respiratory Disease 129: 8-11, 1984.

67. Lebowitz, M., Holberg, C.J., Boyer, B. and Hayes, C., "Respiratory Symptoms and Peak Flow Associated with Indoor and Outdoor Air Pollutants in the Southwest," Journal of the Air Pollution Control Association 35: 1154-1158, 1985.

68. Melia, R., Florey, C.D.V., Altman, D.G. and Swan, A.V., "Association Between Gas Cooking and Respiratory Disease in Children," British Medical Journal II: 149-152, 1977.

69. Melia, R., Florey, C.D.V., Morris, R.W., Goldstein, B.D., John, H.H., Clark, D., Craighead, I.B. and Mackinlay, J.C., "Childhood Respiratory Illness and the Home Environment II. Association Between Respiratory Illness and Nitrogen Dioxide, Temperature and Relative Humidity," International Journal of Epidemiology 11(2): 164-169, 1982.

70. Melia, R., Chinn, S. and Rona, R.J., "Respiratory Illness and Home Environment of Ethnic Groups," British Medical Journal 296: 1438-1441, 1988.

71. Melia, R., Florey, C.D.V. and Chinn, S., "The Relation Between Respiratory Illness in Primary School Children and the Use of Gas for Cooking. I -- Results from a National Survey," International Journal of Epidemiology 8(4): 333-338, 1979.

72. Speizer, F., Ferris, B., Bishop, Y.M.M. and Spengler, J., "Respiratory Disease Rates and Pulmonary Function in Children

2023469016

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Associated with NO_2 Exposure," American Review of Respiratory Disease 121: 3-10, 1980.

73. Jedrychowski, W., Khogali, M. and Karim, M.A., "Height and Lung Function in Preadolescent Children of Kuwaitis and European Origin. The Pilot Survey on Health Effect of Gas Cooking in the Middle-East." In: Indoor Air Quality and Ventilation. London, Selper Ltd., Volume 2, 175-181, 1990.

74. Brunekreef, B., Houthuijs, D., Dijkstra, L. and Soleij, J.S.M., "Indoor Nitrogen Dioxide Exposure and Children's Pulmonary Function," Journal of the Air and Waste Management Association 40(9): 1252-1256, 1990.

75. Koo, L.C., Ho, J.H.C., Matsuki, H., Shimizu, H., Mori, T. and Tominaga, S., "A Comparison of the Prevalence of Respiratory Illnesses Among Nonsmoking Mothers and Their Children in Japan and Hong Kong," American Review of Respiratory Disease 138: 290-295, 1988.

76. Strachan, D. and Elton, R., "Relationship Between Respiratory Morbidity in Children and the Home Environment," Family Practice 3(3): 137-142, 1986.

77. Strachan, D., "Damp Housing and Childhood Asthma: Validation of Reporting of Symptoms," British Medical Journal 297: 1223-1226, 1988.

78. Platt, S.D., Martin, C.J., Hunt, S.M. and Lewis, C.W., "Damp Housing, Mould Growth, and Symptomatic Health State," British Medical Journal 298: 1673-1678, 1989.

79. Brunekreef, B., Dockery, D., Speizer, F.E., Ware, J.H., Spengler, J.D. and Ferris, B.G., "Home Dampness and Respiratory Morbidity in Children," American Review of Respiratory Disease 140: 1363-1367, 1989.

80. Watkins, C., Sittampalam, Y., Morrell, D.C., Leeder, S.R. and Tritton, E., "Patterns of Respiratory Illness in the First Year of Life," British Medical Journal 293: 794-796, 1986.

81. Kerigan, A., Goldsmith, C.H. and Pengelly, L.D., "A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario: Epidemiologic Survey, Design, Methods, and Description of Cohort," American Review of Respiratory Disease 133: 987-993, 1986.

82. Goren, A. and Hellmann, S., "Prevalence of Respiratory Symptoms and Diseases in Schoolchildren Living in a Polluted

2023469017

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

and in a Low Polluted Area in Israel," Environmental Research 45(1): 28-37, 1988.

83. Pope, C., "Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley," American Journal of Public Health 79(5): 623-628, 1989.

84. Frischer, T., Studnicka, M., Hesse, P. and Neumann, M., "Effects of Traffic Emissions on the Airways in Children," Pneumologie 44: 890-891, 1990.

85. Rutishauser, M., Ackermann, U., Braun, C., Gnehm, H.P. and Wanner, H.U., "Significant Association between Outdoor NO_2 and Respiratory Symptoms in Preschool Children," Lung, Supplement 168: 347-352, 1990.

86. Fleming, D., Cochi, S.L., Hightower, A.W. and Broome, C.V., "Childhood Upper Respiratory Tract Infections: To What Degree is Incidence Affected by Day Care Attendance?," Pediatrics 79(1): 55-60, 1987.

87. Hurwitz, E.S., Gunn, W.J., Pinsky, P.F. and Schonberger, L.B., "Risk of Respiratory Illness Associated with Day-Care Attendance: A Nationwide Study," Pediatrics 87(1): 62-69, 1991.

88. Wright, A.L., Holberg, C.J., Martinez, F.D., Morgan, W.J. and Taussig, L.M., "Breast Feeding and Lower Respiratory Tract Illness in the First Year of Life," British Medical Journal 299: 946-949, 1989.

89. Berwick, M., Zagraniski, R.T., Leaderer, B.P. and Stolwijk, J.A., "Respiratory Illness in Children Exposed to Unvented Combustion Sources." In: Indoor Air. Volume 2: Radon, Passive Smoking, Particulates and Housing Epidemiology. B. Berglund, T. Lindvall and J. Sundell (eds.). Stockholm, Swedish Council for Building Research, 255-260, 1984.

90. Osborne, J. and Honicky, R., "Health Effects of Heating With Wood: Chest Illness in Young Children and Indoor Heating with Woodburning Stoves." In: IAQ '89. The Human Equation: Health and Comfort. American Society of Heating, Refrigeration and Air-Conditioning Engineers, and the Society for Occcupational and Environmental Health, San Diego, California, April 17-20, 1989. Abstract.

91. Morris, K., Morganlander, M., Coulehan, J.L., Gahagen, S. and Arena, V.C., "Wood-Burning Stoves and Lower Respiratory Tract Infection in American Indian Children," American Journal of Diseases in Childhood 144: 105-108, 1990.

2023469018

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

92. Nordvall, S., Eriksson, M., Rylander, E. and Schwartz, B., "Sensitization of Children in the Stockholm Area to House Dust Mites," Acta Paediatr Scand 77: 716-720, 1988.

93. Rylander,R., Sorensen, S., Goto, H., Yuasa, K. and Tanaka, S., "The Importance of Endotoxin and Glucan for Symptoms in Sick Buildings." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 157-164, 1989.

94. Kort, H., van Bronswijk, J. and Schober, G., "Moulds, Mites and Moisture: A Preliminary Report on Six Cases of Fungal Damage in Dwellings." In: Present and Future of Indoor Air Quality. C. Bieva, Y. Courtois, M. Govaerts (eds.). Amsterdam, Excerpta Medica, 389-394, 1989.

95. Ownby, D. and McCullough, J., "Passive Exposure to Cigarette Smoke Does Not Increase Allergic Sensitization in Children," Journal of Allergy and Clinical Immunology 82(4): 634-638, 1988.

96. Johnson, C., Ownby, D., Stauchman, C., Blocki, S., Birg, G., Jacobsen, G. and McCullough, J., "Determinants of Immunoglobulin E (IgE) at Birth," American Journal of Epidemiology 132(4): 773-774, 1990.

97. Tager, I.B., "Health Effects of 'Passive Smoking' in Children," Chest 96(5): 1161-1164, 1989.

98. Sneddon, J.M. and Bearpark, T.M., "Indoor Air, Respiratory Health and Pulmonary Function in Children: A Critical Review." In: Indoor Air Quality and Ventilation. London, Selper Ltd., Volume 2, 143-154, 1990.

99. Witorsch, R.J. and Witorsch, P., "A Critical Analysis of the Relationship Between Parental Smoking and Pulmonary Performance in Children," Off. Gesundh.-Wes 51: 78-83, 1989.

100. Rubin, D. and Damus, K., "The Relationship Between Passive Smoking and Child Health: Methodologic Criteria Applied to Prior Studies," Yale Journal of Biological Medicine 61(5): 401-411, 1988.

2023469019

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

"Compromised Individuals": Children

As with studies of adults who have chronic lung problems, the data on parental smoking and its possible effects on children with lung conditions are inconclusive.[1-9] In 1990, German researchers Oldigs, et al., reported that exposing children with bronchial asthma to cigarette smoke sufficient to reach a level of 20 parts per million (ppm) carbon monoxide for one hour did not affect their lung function or bronchial responsiveness.[8] Similarly, Charles Sherman and his co-investigators reported that neither paternal nor maternal smoking "bore an apparent relation to the development of asthma" in a sample of children, aged 5 to 9, enrolled in public and parochial schools in East Boston, Massachusetts in 1974.[9]

A British researcher, Strachan, has implicated damp housing as a potential factor in the development of childhood asthma.[10] After controlling for the possible influence of housing tenure, number of people per room, number of smokers in the household, and gas cooking, he reported that the relationship between damp housing and childhood asthma in his study population remained "highly significant."

Other investigators, Rubin and Gilljam, et al., have suggested that parental smoking might worsen the condition of

2023469020

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

children with cystic fibrosis, a congenital disease usually developing during childhood and causing pulmonary disorders.[11-12] However, these studies are subject to the same uncertainties exemplified by other studies on parental smoking. For example, although Rubin reported an association between parental smoking and decreased nutritional status and growth of children with cystic fibrosis, he conceded that "the possibility cannot be ruled out that social, economic, or other factors determined both the smoking status of the household and the nutritional status of the child."[11]

2023469021

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

"Compromised Individuals": Children

1. Gortmaker, S.L., Walker, D.K., Jacobs, F.H. and Ruch-Ross, H., "Parental Smoking and the Risk of Childhood Asthma," American Journal of Public Health 72(6): 574-579, 1982.

2. Toyoshima, K., Hayashida, M., Yasunami, J., Takamatsu, I., Niwa, H. and Muraoka, T., "Factors Influencing the Prognosis of Wheezy Infants," Journal of Asthma 24(5): 267-270, 1987.

3. Murray, A.B. and Morrison, B.J., "Passive Smoking and the Seasonal Difference of Severity of Asthma in Children," Chest 94(4): 701-708, 1988.

4. Palmieri, M., Longobardi, G., Napolitano, G. and Simonetti, D.M.L., "Parental Smoking and Asthma in Childhood," European Journal of Pediatrics 149: 738-740, 1990.

5. Weitzman, M., Gortmaker, S., Walker, D.K. and Sobol, A., "Maternal Smoking and Childhood Asthma," Pediatrics 85(4): 505-511, 1990.

6. Lilienfeld, D.E., Ehrlich, R.I., Kattan, M., Saltzber, D.S., Grimm, K.T. and Landrigan, P.J., "Passive Smoking and Urinary Continine Levels in Acute and Non-Acute Asthmatics," Abstracts: International Epidemiology Association Twelfth Scientific Meeting, 78, August 5-9, 1990.

7. Young, S., Le Souef, P.N., Geelhoed, G.C., Stick, S.M., Turner, K.J. and Landau, L.I., "The Influence of a Family History of Asthma and Parental Smoking on Airway Responsiveness in Early Infancy," The New England Journal of Medicine 324(17): 1168-1173, 1991.

8. Oldigs, M., Jorres, R. and Magnussen, H., "Acute Effect of Passive Smoking on Lung Function and Airway Responsiveness in Asthmatic Children," Joint Meeting SEP-SEPCR, London, Barbican Centre, September, 1990.

9. Sherman, C.B., Tosteson, T.D., Tager, I.B., Speizer, F.E. and Weiss, S.T., "Early Childhood Predictors of Asthma," American Journal of Epidemiology 132(1): 83-95, 1990.

10. Strachan, D.P., "Damp Housing and Childhood Asthma: Validation of Reporting of Symptoms," British Medical Journal 297: 1223-1226, 1988.

2023469022

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

11. Rubin, B.K., "Exposure of Children with Cystic Fibrosis to Environmental Tobacco Smoke," New England Journal of Medicine 323(12): 782-788, 1990.

12. Gilljam, H., Stenlund, C., Ericsson-Hollsing, A. and Strandvik, B., "Passive Smoking in Cystic Fibrosis," Respiratory Medicine 84(4): 289-291, 1990.

2023469023

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Heart Disease

Assertions regarding a relationship between heart disease and ETS exposure are primarily based on a small number of epidemiological studies which suffer from a variety of serious methodological weaknesses. In total, 11 epidemiological studies have reported data on a possible statistical association between ETS and heart disease incidence or mortality.[1-11] However, nearly two-thirds of these studies -- seven of the 11 -- failed to report a statistically significant association. Of the four studies that claimed to find a statistically significant relationship, [3-5,9] three are very small-scale,[3-4,9] which means that their conclusions are based on only a few cases and, therefore, may not be very reliable. All of these studies suffer from numerous methodological weaknesses, including small sample sizes, potential misclassification of the smoking status of study participants, inadequate assessment of ETS exposure, failure to control adequately for biases stemming from potential confounding variables and failure to confirm causes of death via autopsy or other histological methods.

Despite these scientific weaknesses, several recent literature reviews have concluded that ETS is associated with an increased risk of heart disease and that, in fact, such exposure causes a large number of deaths among ETS exposed nonsmokers each

2023469024

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

year.[12-16] Four of these reviews attempted to make a specific estimate of overall risk based on the combined data from the epidemiologic studies.[12-15] The authors of these reviews generally agreed that ETS exposure is associated with an approximately 30 percent increase in heart disease risk (risk ratio of 1.3). The most recent, and certainly the most widely publicized, of these reviews was written by Stanton Glantz and William Parmley of the University of California, San Francisco.[15] They argued that their estimate of a 30 percent increase in heart disease risk in ETS-exposed nonsmokers translates into 37,000 excess heart disease deaths in the U.S. each year.

The usual basis for overall risk estimates, including the one by Glantz and Parmley, is meta-analysis. This technique is appropriately used only when the underlying studies are very similar and of high quality.[17] In the case of ETS and heart disease, however, the risk estimates are based on the meta-analysis of a small number of epidemiological studies that are highly dissimilar in terms of the methodology used, the study populations and the disease endpoints. Furthermore, the individual studies often suffer from serious methodological and other scientific weaknesses. For these reasons, the validity of any meta-analysis based on these data is highly questionable.

2023469025

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Claims of an association between ETS and heart disease often receive a great deal of publicity. However, there is a serious scientific debate about the basis for such claims. This is reflected in the wide range of reviews by a variety of individuals from several countries and perspectives who have argued that the available data do not allow any conclusions concerning the question of ETS and heart disease.

The earliest reviews dealing with this question appeared even before much of the epidemiological data became available in the early 1980s.[18-20] While they emphasized the near absence of epidemiological studies on ETS and heart disease, they did discuss data available concerning carbon monoxide (CO) and nicotine, which are often claimed to be the primary substances in ETS that lead to cardiovascular damage. The most extensive of these discussions was a 1984 review by two German researchers, who concluded that, at the levels reported for ETS-exposed nonsmokers, "neither CO nor nicotine is likely to play a role in the development and progression of coronary heart disease."[20]

The first major reviews of the epidemiological data on ETS and heart disease appeared in 1986. In that year, the report from the Office of the U.S. Surgeon General examined the available data and judged that "no firm conclusion" could be made regarding a possible relationship between ETS and heart disease.[21] Also in

2023469026

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

1986, the NAS Report stated that any potential heart disease risk related to ETS would be "difficult to detect or estimate reliably" from epidemiological studies, and would be "the same order of magnitude as what might arise from expected residual confounding due to unmeasured covariates."[22]

As additional epidemiological data on ETS and heart disease have been published, subsequent evaluations have often reinforced the positions of these two reports. There are many examples. In 1988, a review from two scientists at the University of California - Los Angeles, which generally argued that ETS is associated with a disease risk in nonsmokers, nevertheless commented that for heart disease, "no firm conclusion that a causal relation exists is yet warranted."[23] A similar view was expressed in a 1988 review from a Harvard physician, who said that there were "no clear data" that ETS increases heart disease risk.[24] Both of these reviews called for more research.

Following a detailed discussion of the recent epidemiological studies on ETS and heart disease at the ETS conference held at McGill University, a New York Medical College faculty member concluded that "none" of the studies "provides any basis for altering the Surgeon General's and NAS's conclusions concerning ETS and cardiovascular disease."[25]

2023469027

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Several additional evaluations of the literature on ETS and heart disease appeared in 1990. Two of these were reported at international conferences in Lisbon, Portugal[26] and in Budapest, Hungary.[27] Both argued strongly that the data on ETS and heart disease were methodologically weak and insufficient to draw conclusions. A third, by a physician from a hospital and medical school in Dundee, Scotland, was in the context of a broad review of many factors potentially involved in heart disease.[28] Although he argued that smoking cigarettes is a risk factor and cause of death among smokers, he nevertheless suggested that attempts to attribute heart disease deaths to ETS exposure "may be pushing epidemiologic evidence to the limits of what it can show." In another major review, this one from the United States, two physicians concluded that "the data that are available are so sparse that any attempt to reach a definitive assessment would be fraught with uncertainty."[29]

Perhaps the most recent review of the literature on ETS and heart disease was published in 1991 by the former director of toxicology of a major European research laboratory. He described the scientific data relating to a possible heart disease risk in nonsmokers exposed to ETS as "not very convincing."[30]

Several evaluations of the literature on the ETS and heart disease have been prepared under the auspices of a number of

2023469028

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

national governments. As with the 1986 U.S. Surgeon General's Report,[21] they often voice strong opinions that smoking and ETS exposure are associated with serious health risks. Nevertheless, they argue that the data on ETS as a possible cause of heart disease are inconclusive. For example, in 1987, reports dealing with ETS were issued by Canada's Minister of National Health and Welfare[31] and by Australia's National Health and Medical Research Council.[32] Both reports described the data as "limited" and inadequate to permit a conclusion to be drawn.

European government reports have also expressed similar concessionary opinions concerning ETS and heart disease. In 1990, a Committee of the Health Council of the Netherlands prepared a report at the request of the Dutch government. The Committee judged that the "currently available data preclude a firm conclusion as to whether exposure to tobacco smoke is a contributory factor in the onset of and mortality from cardiovascular disease in nonsmokers."[33] In Norway, a Report from a Working Group appointed by the Norwegian Directorate of Health also examined this issue. Although the report acknowledged there are data suggesting a statistical association between ETS and heart disease, it judged that "no definite causal connection can be ascertained at the present."[34]

2023469029

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Heart Disease: Experimental/Biochemical Studies

In addition to the epidemiological studies, there are several experimental and biochemical studies that have been cited as supporting an increase in heart disease risk stemming from ETS exposure. A few of these reports claim that ETS exposure adversely affects exercise capacity[35-37] and that, in the case of heart disease patients, this can lead to attacks of angina (heart pain).[36-37] Other reports have attempted to demonstrate that exposure to ETS adversely affects some aspect of cardiovascular function, particularly blood clotting[38-41] and cholesterol levels.[42-43]

In the area of exercise performance, three studies are generally cited. In one of these, a 1985 report by McMurray, et al., ETS exposure was claimed to adversely affect the exercise performance of healthy subjects.[35] In the two other studies, one by Aronow[36] and the other by Khalfen and Klochkov,[37] heart disease patients exposed to ETS reportedly were unable to exercise as long before experiencing angina. The credibility of the Aronow report, as well as other research by this investigator, has been widely challenged.[44-47] The Khalfen and Klochkov report is a Russian language article about which relatively little is known. Regarding any of these studies, whether conducted with healthy subjects or heart disease patients, the general criticism can be made that it

2023469030

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

is almost impossible to "blind" either the experimenter or the subjects to ETS exposure. Thus, there is always the possibility that some subjective psychological factor may have influenced the results.

There are very limited data attempting to demonstrate that ETS adversely affects some process that might be involved in blood clotting or atherosclerosis. The hypothesis of the studies from which these data are derived has been that ETS may increase the tendency of certain blood components, known as platelets, to stick together. This claim has been made based mainly on data in four published reports,[38-41] three of which are from the same Austrian research group.[38-40] The fourth report, from a group of researchers in Kansas City, Missouri,[41] suffers from serious methodological weaknesses, particularly its failure to establish a proper control for comparison purposes.

Finally, there are two reports which assessed cholesterol and other blood components among children in relation to parental smoking status.[42-43] Both reports claim that parental smoking is associated with decreases in HDL (high density lipoprotein) cholesterol, which some have argued may be associated with heart disease risk. These studies measured components of blood as the endpoint, but are essentially epidemiological studies in that they, at best, may suggest statistical associations. As such, they suffer

2023469031

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

from weaknesses characteristic of other epidemiological studies of ETS exposure, especially difficulties in controlling for potential confounding variables and inadequate assessment of ETS exposure. Furthermore, the potential significance of blood values in relation to later heart disease risk in a group of children is highly speculative.

2023469032

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Heart Disease

1. Butler, T., "The Relationship of Passive Smoking to Various Health Outcomes Among Seventh-Day Adventists in California," Presentation at the Seventh World Conference on Tobacco and Health, 1990. Abstract.

2. Garland, C., Barrett-Connor, E., Suarez, L., Criqui, M.H. and Wingard, D.L., "Effects of Passive Smoking on Ischemic Heart Disease Mortality of Nonsmokers: A Prospective Study," American Journal of Epidemiology 121(5): 645-650, 1985.

   Garland, C., Barrett-Connor, E., Suarez, L., Criqui, M.H. and Wingard, D.L., "Effects of Passive Smoking on Ischemic Heart Disease Mortality of Nonsmokers: A Prospective Study," Erratum, American Journal of Epidemiology 122: 1112, 1985.

3. Gillis, C.R., Hole, D.J., Hawthorne, V.M. and Boyle, P., "The Effect of Environmental Tobacco Smoke in Two Urban Communities in the West of Scotland." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 121-126, 1984.

   Hole, D.J., Gillis, C.R., Chopra, C. and Hawthorne, V.M., "Passive Smoking and Cardiorespiratory Health in a General Population in the West of Scotland," British Medical Journal 299: 423-427, 1989.

4. He, Y., et al., "Women's Passive Smoking and Coronary Heart Disease," Chung Hua Yu Fang I Hsueh Tsa Chih 23(1): 19-22, 1989.

5. Helsing, K.J., Sandler, D.P., Comstock, G.W. and Chee, E., "Heart Disease Mortality in Nonsmokers Living With Smokers," American Journal of Epidemiology 127(5): 915-922, 1988.

   Sandler, D.P., Comstock, G.W., Helsing, K.J. and Shore, D.L., "Deaths from All Causes in Non-Smokers Who Lived with Smokers," American Journal of Public Health 79(2): 163-167, 1989.

6. Hirayama, T., "Lung Cancer in Japan: Effects of Nutrition and Passive Smoking." In: Lung Cancer: Causes and Prevention. M. Mizell and P. Correa (eds.). New York, Verlag Chemie International, Chapter 14, 175-195, 1984.

2023469033

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

7. Humble, C., Croft, J., Gerber, A., Casper, M., Hames, C.G. and Tyroler, H.A., "Passive Smoking and 20-Year Cardiovascular Disease Mortality among Nonsmoking Wives, Evans County, Georgia," American Journal of Public Health 80(5): 599-601, 1990.

8. Lee, P.N., Chamberlain, J. and Alderson, M.R., "Relationship of Passive Smoking to Risk of Lung Cancer and Other Smoking-Associated Diseases," British Journal of Cancer 54: 97-105, 1986.

9. Martin, M.J., Hunt, S.C. and Williams, R.R., "Increased Incidence of Heart Attacks in Nonsmoking Women Married to Smokers," Presentation at the Annual Meeting of the American Public Health Association, 1986. Abstract.

10. Palmer, J.R., Rosenberg, L. and Shapiro, S., "Passive Smoking and Myocardial Infarction in Women," CVD Epidemiology Newsletter No. 43, 29, Winter 1988. Abstract.

11. Svendsen, K.H., Kuller, L.H., Martin, M.J. and Ockene, J.K., "Effects of Passive Smoking in the Multiple Risk Factor Intervention Trial," American Journal of Epidemiology 126(5): 783-795, 1987.

12. Wells, A.J., "An Estimate of Adult Mortality in the United States from Passive Smoking," Environment International 14(3): 249-265, 1988.

13. Kawachi, I., Pearce, N.E. and Jackson, R.T., "Deaths from Lung Cancer and Ischaemic Heart Disease Due to Passive Smoking in New Zealand," New Zealand Medical Journal 102(871): 337-340, 1989.

14. Kristensen, T.S., "Cardiovascular Diseases and the Work Environment. A Critical Review of the Epidemiologic Literature on Chemical Factors," Scand. J. Work Environ. Health 15: 245-264, 1989.

15. Glantz, S.A. and Parmley, W.W., "Passive Smoking and Heart Disease: Epidemiology, Physiology, and Biochemistry," Circulation 83(1): 1-12, 1991.

16. Beaglehole, R., "Does Passive Smoking Cause Heart Disease?," British Medical Journal 301: 1343-1344, 1990.

17. Fleiss, J.L. and Gross, A.J., "Meta-Analysis in Epidemiology, with Special Reference to Studies of the Association Between Exposure to Environmental Tobacco Smoke and Lung Cancer: A

2023469034

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Critique," Journal of Clinical Epidemiology 44(2): 127-139, 1991.

18. Frishman, W.H., "Involuntary Smoking: Cardiovascular Effects of Smoke on Nonsmokers," Cardiovascular Medicine 4(3): 289-291, 296, 1979.

19. Kannel, W.B., "Update on the Role of Cigarette Smoking in Coronary Artery Disease," American Heart Journal 101(3): 319-328, 1981.

20. Schievelbein, H. and Richter, F., "The Influence of Passive Smoking on the Cardiovascular System," Preventive Medicine 13: 626-644, 1984.

21. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

22. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

23. Fielding, J.E. and Phenow, K.J., "Health Effects of Involuntary Smoking," The New England Journal of Medicine 319(22): 1452-1460, 1988.

24. Weiss, S.T., "What are the Health Effects of Passive Smoking?" The Journal of Respiratory Diseases 9(1): 46-48, 55, 58, 60, 62, 1988.

25. Wexler, L.M., "Environmental Tobacco Smoke and Cardiovascular Disease: A Critique of the Epidemiological Literature and Recommendations for Future Research." In: Environmental Tobacco Smoke: Proceedings of the International Symposium at McGill University 1989. D.J. Ecobichon and J.M. Wu (eds.). Lexington, Massachusetts, Lexington Books, D.C. Heath and Company, Chapter 8, 139-152, 1990.

26. Weetman, D.F. and Munby, J., "Environmental Tobacco Smoke (ETS) and Cardiovascular Disease." In: Indoor Air Quality and Ventilation. F. Lunau and G.L. Reynolds (eds.). London, Selper Ltd., 211-216, 1990.

27. Thiery, J. and Cremer, P., "Coronary Heart Disease and Involuntary Smoking," The Toxicology Forum: 1990 European

2023469035

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Meeting, Session on "Environmental Tobacco Smoke: Science and Meta-Science," Budapest, Hungary, June 19, 1990.

28. Tunstall-Pedoe, H., "Epidemiology and Prevention of Ischemic Heart Disease," Current Opinion in Cardiology 5: 379-386, 1990.

29. Mahajan, V.K. and Huber, G.L., "Health Effects of Involuntary Smoking: Impact on Tobacco Use, Smoking Cessation, and Public Policies," Seminars in Respiratory Medicine 11(1): 87-114, 1990.

30. Armitage, A.K., "Environmental Tobacco Smoke and Coronary Heart Disease." In: Other People's Tobacco Smoke. A.K. Armitage (ed.). Beverly, East Yorks, United Kingdom, Galen Press, Chapter 7, 109-116, 1991.

31. Department of National Health and Welfare, Environmental Health Directorate, Health Protection Branch, Involuntary Exposure to Tobacco Smoke. Ottawa, Canada, Environmental Health Directorate, Publications No. 87-EHD-138, 1987.

32. National Health and Medical Research Council, "Passive Smoking and Cardiovascular Disease." In: Effects of Passive Smoking on Health. Report of the NHMRC Working Party on the Effects of Passive Smoking on Health. Canberra, Australian Government Printing Service, Chapter 8, pp. 38-42, 1987.

33. Health Council Committee on Passive Smoking, "Passive Smoking. Assessment of the Harmfulness to Health of Environmental Tobacco Smoke: Report of the Health Council Committee on Passive Smoking to the Minister and State Secretary for Welfare, Health and Cultural Affairs," The Hague, Netherlands, No. 1990/18, December 10, 1990. Translation.

34. Working Group Appointed by the Norwegian Directorate of Health, Recommendations for Indoor Air Quality, Extracts from Health Directorate Report Series 6-90, Report No. 5/90, IK-2322, July 1990. Translation.

35. McMurray, R.G., Hicks, L.L. and Thompson, D.L., "The Effects of Passive Inhalation of Cigarette Smoke on Exercise Performance," European Journal of Applied Physiology 54(2): 196-200, 1985.

36. Aronow, W.S., "Effect of Passive Smoking on Angina Pectoris," New England Journal of Medicine 299(1): 21-24, 1978.

2023469036

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

37. Khalfen, E.Sh. and Klochkov, V.A., "Effect of 'Passive' Smoking on the Physical Load Tolerance of Coronary Heart Disease Patients," Ter Arkh 5: 112-115, 1987. Translation.

38. Sinzinger, H. and Kefalides, A., "Passive Smoking Severely Decreases Platelet Sensitivity to Antiaggregatory Prostaglandins," Letter, Lancet II: 392-393, August 14, 1982.

39. Burghuber, O.C., Punzengruber, Ch., Sinzinger, H., Haber, P. and Silberbauer, K., "Platelet Sensitivity to Prostacyclin in Smokers and Non-smokers," Chest 90(1): 34-38, 1986.

40. Sinzinger, H. and Virgolini, I., "Are Passive Smokers at Greater Risk of Thrombosis?" Wiener Klinische Wochenschrift 20: 649-698, 1989. Translation.

41. Davis, J.W., Shelton, L., Watanabe, I.S. and Arnold, J., "Passive Smoking Affects Endothelium and Platelets," Arch Intern Med 149: 386-389, 1989.

42. Moskowitz, W.B., Mosteller, M., Schiekern, R.M., Bossano, R., Hewitt, J.K., Bodurtha, J.N. and Segrest, J.P., "Lipoprotein and Oxygen Transport Alterations in Passive Smoking Preadolescent Children: The MCV Twin Study," Circulation 81(2): 586-592, 1990.

43. Pomrehn, P., Hollarbush, J., Clarke, W. and Lauer, R., "Children's HDL--chol: The Effects of Tobacco; Smoking, Smokeless and Parental Smoking," Circulation 81(2): 720, 1990. Abstract.

44. Fisher, E., Statement, U.S. Congress, House Committee on Agriculture, Subcommittee on Tobacco, Effect of Smoking on Nonsmokers, Hearing, 95th Congress, 2nd Session, Washington, D.C., U.S. Government Printing Office, 35-40, September 7, 1978.

45. Shephard, R., The Risks of Passive Smoking, London, Croom-Helm Ltd., 73, 1982.

46. Mintz, M., "FDA, Citing Phony Evidence, Bars Drug Tests by Researcher," The Washington Post, March 23, 1983.

47. Peterson, C., "EPA Probe Criticizes a Study Used in Air Quality Standard," The Washington Post, June 7, 1983.

2023469037

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Other Children's Diseases and Conditions/Pregnancy

There are studies which claim to have found an association between exposure to ETS and the occurrence of a relatively common childhood ear condition called otitis media with effusion (OME) and the incidence of low birth weight infants.[1-3] However, as with other claims regarding ETS, the reported data are inconsistent, even contradictory, in nature.

For example, in regard to OME, an inflammation of the inner ear that can lead to the effusion or accumulation of fluid in the inner ear canal, a group of Dutch researchers has asserted that "there is little evidence that parental smoking has an effect on the risk for OME," although they noted that "the literature is not consistent."[4] Their own study indicated that while the occurrence of OME was not related to exposure to ETS in the home, variables relating to age, season, family size, sibling's history of OM, frequent swimming, and public day care attendance had a "significant effect." A Scottish study which did report an association between parental smoking and OME noted that the prevalence of parental smoking was higher in rented or crowded homes, and in homes affected by dampness or mould growth.[2] Clearly, these reports suggest there is a need to evaluate additional factors in any study of the relationship between OME and parental smoking.

2023469038

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Other researchers recently acknowledged that questionnaire reports of acute OME may be an inadequate method of determining the incidence of the condition in epidemiological studies.[5] Therefore, until a more accurate method of determining the incidence of OME is found, isolating parental smoking as a cause is seemingly unjustified.

In regard to infant birthweight, a 1986 study by Rubin, et al., reported that infants with smoking fathers had lower birthweights compared to those with nonsmoking fathers.[3] However, the results were described as "extraordinarily large" by one reviewer, apparently because the authors failed to control for important confounding variables such as social class.[6] Moreover, a study published in 1987 reported results which contradicted those of Rubin, et al. The authors, MacArthur and Knox, observed that the average weight of infants with smoking fathers was greater than that of infants with non-smoking fathers.[7] Still other studies have reported no significant association between paternal smoking and lower birthweight among newborn infants,[8-11] although one study did report an association with the overall condition of the infant at birth.[10] However, this may be due to some unaccounted for factor. The potential importance of such factors is indicated by a 1990 report of one study which noted that, after adjusting for 57 different confounding factors, paternal smoking had no statistically significant effect on infant birthweight.[11]

2023469039

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Reports that parental smoking causes otitis media in children and reduces infant birthweight are contradicted by studies reporting no association between parental smoking and OME or infant birthweight. In addition, the methods used in these studies to determine exposure to ETS and the incidence of OME are seemingly inaccurate. Thus, the role, if any, of parental smoking has yet to be determined.

2023469040

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Other Children's Diseases and Conditions

1. Kraemer, M., Richardson, M.A., Weiss, N.S., Furukawa, C.T., Shapiro, G.G., Pierson, W.E. and Bierman, C.W., "Risk Factors for Persistent Middle Ear Effusions: Otitis Media, Catarrh, Cigarette Smoke Exposure, and Atopy," Journal of the American Medical Association 249(8): 1022-1025, 1983.

2. Strachan, D.P., "Impedance Tympanometry and the Home Environment in Seven-Year-Old Children," The Journal of Laryngology and Otology 104: 4-8, 1990.

3. Rubin, D., Krasilnikoff, P.A., Leventhal, J.M., Weile, B., and Berget, A., "Effect of Passive Smoking on Birth-Weight," Lancet II: 415-417, 1986.

4. Zielhuis, G.A., Heuvelmans-Heinen, E.W., Rach, G.H. and Van Den Broek, P., "Environmental Risk Factors for Otitis Media with Effusion in Preschool Children," Scandinavian Journal of Primary Health Care 7(1): 33-38, 1989.

5. Alho, O.P., "The Validity of Questionnaire Reports of a History of Acute Otitis Media," American Journal of Epidemiology 132(6): 1164-1170, 1990.

6. Trichopoulos, D., "Passive Smoking, Birthweight, and Oestrogens," Lancet II: 743, 1986.

7. MacArthur, C., and Knox, E., "Passive Smoking and Birthweight," Lancet I(8523): 37-38, 1987.

8. Little, R. and Sing, C., "Father's Drinking and Infant Birth Weight: Report of an Association," Teratology 36: 59-65, 1987.

9. Chen, Y., Pederson, L.L., and Lefcoe, N.M., "Passive Smoking and Low Birthweight," Lancet II: 54-55, 1989.

10. Kikuchi, S. and Takahashi, T., "Effect of Paternal Smoking on Fetuses." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 272-277, 1990.

11. Rantakallio, P., Hartikainen-Sorri, A.L. and Leino, T., "The Effect of Parental Smoking and Industrial Pollution on Birth Weight." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 219-225, 1990.

2023469041

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Allergy

Although some individuals are annoyed by the sight and smell of tobacco smoke and a few even report experiencing irritation, the existence of human allergens in tobacco smoke has not been established scientifically. This is an extremely important point in the ETS debate because those seeking to ban smoking in public places have often done so by claiming that nonsmokers are "allergic" to tobacco smoke.

However, a number of research groups have been unable to conclude that humans actually experience a true tobacco smoke allergy.[1-6] In 1980, for example, a group of researchers noted that "direct evidence that tobacco smoke is immunogenic [capable of evoking a specific response] in man is yet to be documented."[5] A more recent report by this same group affirms this conclusion.[6]

Claims about a human tobacco allergy stem primarily from studies in which tobacco leaf extract has been reported to cause allergic skin responses in some people, usually in those who already experience allergic reactions to other substances such as weeds.[7-9] However, as an English immunologist pointed out, there are "great difficulties" in determining whether positive reactions to tobacco leaf extracts are relevant to clinical responses to tobacco smoke.[4] Although he noted that there may be substances in tobacco smoke

2023469042

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

which could "theoretically" act as such agents, he concluded that "there is no proof that the specific sensitization to tobacco smoke exists."

It has also been hypothesized that tobacco smoke is capable of provoking an asthma attack as an allergic reaction.[10-11] However, a Swedish specialist concluded that such results are not proof of a tobacco allergy because the studies, which used tobacco extracts, did not differentiate between non-specific and true allergic reactions in evaluating the results of skin tests and bronchial provocation.[12] Consequently, he stated, "for the present, the question as to whether allergy to cigarette smoke exists or not should be kept open." Other research affirms this point. Scientists reported in 1988 that tobacco leaf sensitivity was not associated with decreased pulmonary function in allergic asthmatics.[13]

Certainly, there appear to be people who may be sensitive to tobacco smoke, but personal annoyance and emotional reactions should not be confused with genuine allergic reactions. In many cases, the individual may be responding to high room temperatures, lack of ventilation, or even to the mere sight of tobacco smoke. Indeed, Dr. John Salvaggio, the director of an allergic disease center in the U.S., has suggested that reported reactions to tobacco smoke may be irritative rather than allergic. After reviewing the

2023469043

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

studies on the allergy question, he concluded that "there is no proof that tobacco smoke is allergenic in man."[14]

Accordingly, it is not surprising that researchers at the Mayo Clinic failed to find any evidence of tobacco smoke allergies in their tests of subjects who considered themselves allergic to tobacco and tobacco smoke.[15] It has been reported in other studies that people who claim to be "smoke sensitive" did not react more frequently to tobacco leaf or smoke extract than those who are "smoke resistant."[13,16]

On the basis of these data, it must be questioned what people really mean when they say they are "allergic" to tobacco smoke. It may be that they simply do not like the sight and smell of tobacco smoke and are interpreting their reaction to mean that they are "allergic" to environmental tobacco smoke. But, as has been pointed out, such personal reactions should <u>not</u> be regarded as true tobacco smoke allergies.

2023469044

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Allergy

1. Justus, D. and D. Adams, "Evaluation of Tobacco Hypersensitivity Responses in the Mouse: A Potential Animal Model for Critical Study of Tobacco Allergy," Int Arch Allergy Appl Immunol 51(6): 687-695, 1976.

2. Lehrer, S., et al., "Immunochemical Properties of Tobacco Smoke and Leaf Components," Fed Proc 37(6): 1456, 1978.

3. Lehrer, S., et al., "Immunogenic Properties of Tobacco Smoke," J Allerg Clin Immunol 62(6): 368-370, 1978.

4. Taylor, G., "Tobacco Smoke Allergy -- Does It Exist?" In: Environmental Tobacco Smoke Effects on the Nonsmoker: Report from a Workshop. R. Rylander (ed.). Published in Scand J Respir Dis Supplement 91: 50-55, 1974.

5. Lehrer, S., et al., "Immunogenicity of Tobacco Smoke Components in Rabbits and Mice," Int Arch Allergy Appl Immunol 62: 16-22, 1980.

6. Lehrer, S., et al., "Tobacco Smoke Sensitivity: A Result of Allergy?," Ann Allergy 56: 1-10, 1986.

7. Gleich, G., et al., "Allergy to Tobacco Antigens," J Allerg Clin Immunol 63(3): 211-212, 1979.

8. Harkavy, J., "Tobacco Allergy in Cardiovascular Disease: A Review," Ann Allerg 26: 447-459, 1968.

9. Speer, F., "Tobacco and the Nonsmoker: A Study of Subjective Symptoms," Arch Environ Health 16(3): 443-446, 1968.

10. Stahle, I. and L. Tibbling, "Tobaksallergi hos Patienter Med Asthma Bronchiale (Tobacco Allergy Among Patients with Bronchial Asthma)," Lakartidningen 75(17): 1711-1713, 1978. Translation.

11. Tibbling, L., "Elicitation of Bronchial Asthma with Tobacco Extract," Abstracts of the 4th World Conference on Smoking and Health, Stockholm, Sweden, June 18-21, 1979.

12. Bylin, G., "Tobaksallergi -- finns den? (Tobacco Allergy -- Does It Exist?)," Lakartidningen 77(16): 1530-1532, 1980. Translation.

2023469045

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

13. Stankus, R. and S. Lehrer, "Inhalation Challenge Studies on Tobacco Smoke Sensitive Asthmatics." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 303-304, 1988.

14. Salvaggio, J., Statement, U.S. Congress Committee on Agriculture, Subcommittee on Tobacco, Effect of Smoking on Nonsmokers, Hearing, 95th Congress, 2nd Session, Washington, D.C., U.S. Government Printing Office, 46-49, September 7, 1978.

15. McDougall, J. and G. Gleich, "Tobacco Allergy -- Fact or Fancy?," J Allerg Clin Immunol 57(3): 237, 1976. Abstract.

16. Lehrer, S., et al., "Immunological Evaluation of Tobacco Smoke 'Sensitive' Individuals by Skin, Radioallergosorbent and Precipitin Tests," J Allerg Clin Immunol 67: 49, 1981. Abstract.

2023469046

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Sick Building Syndrome

Advocates of smoking restrictions in the workplace argue that ETS exposure gives rise to a number of complaints, including headaches, nausea, coughs, sore eyes and breathing difficulties. However, research indicates that this complex pattern of symptoms, the so-called "sick building syndrome," is commonly reported in modern office buildings whether or not smokers are present.[1-4]

The reported findings of several Canadian investigators demonstrate this point. In 1983, two of these researchers reported on their extensive review of over 150 indoor air quality evaluations of office buildings compiled by U.S. government agencies, universities and others.[5] After examining the data collected during these evaluations, they concluded that smoking did not significantly affect either indoor atmospheres or the frequency of worker complaints and symptoms:

> The review of available studies does not provide any objective evidence that either pollution levels or patterns of health related complaints differ in some remarkable way between locations with or without smoking restrictions.

They did observe that "inadequate" ventilation creates conditions "where discomfort and illness result irrespective of whether or not smoking is permitted." These observations were reaffirmed in

2023469047

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

reports published in 1987 and 1989.[4,6] In their 1989 report, the researchers noted that smoking was related to complaints in only 12 of 408 (less than three percent) of the building investigations included in the database.

Government investigators with Health and Welfare Canada (HWC), in their report on 94 building studies, also noted that only five percent of the complaints were attributable to indoor constituents such as photocopy machine emissions and ETS.[3] In a 1990 update, these investigators reported on data from a total of 1,362 building investigations. Inadequate ventilation was identified as a problem in 52 percent of the buildings.[7]

Similarly, researchers with the U.S. National Institute of Occupational Safety and Health (NIOSH), in a review of 203 air quality investigations of government and business offices, schools and health care facilities, concluded that tobacco smoke played a contributing role in only four (two percent) of the building complaints investigated.[1] A large majority of the complaints were traced to general building contamination and inadequate ventilation. Recently, NIOSH officials reported on an additional 326 building investigations conducted by the agency through 1988.[8] Over one-half of the investigations revealed inadequate ventilation as the source of complaints.

2023469048

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In 1988, a representative of a U.S. firm specializing in the maintenance of office air conditioning and heating systems reported on 223 individual indoor air quality investigations of publicly and privately owned office buildings.[2] As in the NIOSH investigations, ETS was implicated in only four percent of the buildings investigated. He stated that the majority of indoor air quality problems in modern office buildings may be traced to inadequate fresh air circulation and to poorly maintained ventilation systems which act as breeding grounds for fungi, bacteria and other contaminants. He also suggested that visible tobacco smoke ought to be considered a symptom, rather than a cause, of general indoor air quality problems, in that ETS is often the only visible sign that a ventilation problem exists.

In 1990, investigators from the same firm reported on a survey of 26 commercial office buildings in 20 cities in Switzerland.[9] Unacceptably low ventilation rates were reported in more than half of the buildings investigated. ETS was associated with complaints in only six buildings, all of which also were affected by inadequate ventilation. Acceptable ventilation rates, according to the researchers, resulted in low levels of ETS constituents.

It is perhaps understandable, given the easy recognition of ETS, that persons experiencing sick building symptoms tend to

2023469049

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

blame ETS. Indeed, researchers have verified that the mere visibility or presence of tobacco smoke may provoke claims that ETS is the cause of reported symptoms and complaints.[10-11] However, removal of ETS through smoking bans may serve only to divert attention from more basic, underlying indoor air quality problems. As one commentator pointed out: "Removing the smoker entirely, then, may not affect health and comfort problems in 95% to 98% of sick buildings."[12]

Summary

The foregoing review illustrates the inconsistent and inconclusive nature of the data regarding claims about ETS exposure and disease in nonsmokers. Many of the reports relied upon by those who claim that ETS exposure is associated with disease in nonsmokers are epidemiologic studies that report relative risks which are deemed "weak" and rarely achieve statistical significance. The data in such studies are consistent with the hypothesis that there is no association between ETS exposure and disease. Many of those same studies invariably fail to consider other variables associated with disease, e.g., heredity, (poor) diet, occupational exposures, cross-infections, exposures to indoor and outdoor air pollution, etc. Moreover, nonsmoker exposures to ETS have not been directly assessed in any of the epidemiologic reports. Instead, kinds and amounts of exposure are assessed via

2023469050

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

questionnaire and depend upon recall by cases, next-of-kin and friends. This method is inherently crude and may lead to inaccuracies in exposure assessment. However, a large body of data from actual ETS measurements in the indoor environment exists. These data are examined in detail in the following section.

2023469051

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

Sick Building Syndrome

1. Melius, J., et al., "Indoor Air Quality -- the NIOSH Experience," Ann Am Conf Gov Ind Hyg 10: 3-7, 1984.

2. Robertson, G., "Source, Nature and Symptomology on Indoor Air Pollutants." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 311-319, 1988.

3. Kirkbride, J., Sick Building Syndrome: Causes and Effects, Health and Welfare Canada, Ottawa, Canada, October 24, 1985.

4. Collett, C. et al., "A Database of Problem Buildings: Learning by Past Mistakes." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Amsterdam, Elsevier Science Publishers, 413-419, 1989.

5. Sterling, T. and E. Sterling, "Investigations on the Effect of Regulating Smoking on Levels on Indoor Pollution and on the Perception of Health and Comfort of Office Workers." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement No. 133, Vol. 65, 17-31, 1984.

6. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," J Occup Med 29(1): 57-62, 1987.

7. Kirkbride, J., et al., "Health and Welfare Canada's Experience in Indoor Air Quality Investigation." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 5, 99-106, July 29-August 3, 1990.

8. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer, "The NIOSH Approach to Conducting Indoor Air Quality Investigations in Office Buildings," Indoor Air Quality Selected References, September, 1989.

9. Turner, S. and P. Binnie, "An Indoor Air Quality Survey of Twenty-Six Swiss Office Buildings." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air

2023469052

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Quality and Climate. Toronto, Canada, Volume 4, 27-32, July 29-August 3, 1990.

10. Pimm, P., et al., "Physiological Effects of Acute Passive Exposure to Cigarette Smoke," Arch Environ Health 33(4): 201-213, 1978.

11. Winneke, G. et al., "Psychophysiological Response to Environmental Tobacco Smoke in an Experimental Social Setting." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 173-183, 1990.

12. Sterling, T. and S. Kleven, "The Epidemiology of 'Sick Public Buildings'." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 79-96, 1989.

2023469053

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

III. ENVIRONMENTAL TOBACCO SMOKE AND INDOOR AIR QUALITY

It is often suggested that ETS is a major source of indoor pollution. However, the scientific literature indicates that, except under experimental or other extraordinary conditions, ETS does not have a significant influence on the quality of indoor air.[1-3] The claim that ETS is a significant source of indoor air pollution (and, as such, poses an increased risk for disease among nonsmokers) is based upon several unwarranted assumptions and misrepresentations of the scientific data. This becomes apparent in an analysis of the ETS/indoor air quality question, which addresses the nature and makeup of ETS, its contribution to indoor air, and the methods employed to measure exposure to it.

Sidestream Smoke

It is frequently claimed that sidestream smoke (SS), or the smoke from the burning end of the cigarette, contains much higher amounts of certain constituents than mainstream smoke (MS), or the smoke to which the smoker is exposed. Such a claim implies that a nonsmoker is at increased risk of disease because of his exposure to sidestream smoke, which has more allegedly "toxic" or harmful constituents than mainstream smoke. However, this argument is extremely misleading for several reasons, most notably because it fails to take into account that sidestream smoke is immediately

2023469054

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

diluted in the surrounding air. This diluted sidestream and exhaled mainstream smoke is more accurately called "ETS."

ETS differs chemically and physically from both mainstream and sidestream smoke.[4-9] ETS is a dynamic, ever-changing mixture which undergoes chemical reactions and physical changes as it ages and dissipates. Decay or disintegration patterns for ETS constituents vary over time and are dependent upon environmental features including air currents and attraction to surfaces, such as walls. In addition, reports indicate that constituents in ETS are hundreds to thousands of times more diluted than those identified in either SS or MS.[10-11] In fact, concentrations of ETS constituents in indoor settings frequently fall below detection limits of current scientific measurement devices.[12-16]

Many studies and reviews on ETS employ sidestream/mainstream smoke comparisons, ostensibly to demonstrate the kind and quantity of ETS constituents to which the nonsmoker is exposed. However, such comparisons are deceptive and misleading, as researchers on tobacco smoke chemistry reported in 1990:

> Although ETS originates from sidestream and exhaled mainstream smoke, the great dilution and other changes which these smoke streams undergo as they form ETS make their properties significantly different from those of ETS. Thus, the sidestream/mainstream ratios quoted . . . can be misleading if used out of context. The important question is not the

2023469055

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

ratio of sidestream/mainstream but rather what is the concentration of the constituent in the indoor environment and how does it compare to levels from sources other than ETS. Studies based solely on observations of fresh sidestream, or highly and unrealistically concentrated ETS, should take into account the possible differences between these smokes and ETS found in real-life situations.[4]

Thus, it is both inappropriate and misleading to suggest that sidestream smoke is equivalent to ETS and that, under ordinary conditions, the nonsmoker is exposed to the levels of constituents reported in sidestream smoke.

Biological Markers

Some reports have suggested that the potential toxicity of ETS can be assessed by measuring the body fluids of nonsmokers exposed to ETS for mutagens, which are substances capable of altering the genetic structure of cells.[17-19] It is suggested that the presence of mutagens in body fluids, such as urine, may indicate that an individual has been exposed to substances capable of inducing cancer. These studies, however, did not employ realistic levels of exposure to ETS. Nor did they control adequately for the presence of mutagenic substances in the diet of the study subjects. Studies which have compared mutagens in the body fluids of nonsmokers exposed to realistic levels of ETS and nonsmokers not exposed to ETS report no significant difference in

2023469056

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

mutagenic activity.[20-23]

It is argued that sidestream smoke (and by inference, ETS) contains polycyclic aromatic hydrocarbons (PAHs), substances which have been designated as carcinogens or cancer-causing by various governmental agencies. However, in a series of papers, German researchers reported finding no significant differences in urinary PAH by-products between nonsmokers exposed to ETS and those not exposed.[24-26] Diet, on the other hand, was reported to have a profound influence on PAH by-product formation in all the study subjects.

It has also been suggested that DNA adducts can be utilized as biomarkers to assess exposure to ETS. (An adduct is a product derived from reactions between chemicals and biological material, such as DNA, the genetic material in the body). Research, however, does not support this theory; nonsmokers exposed to ETS do not appear to exhibit increased DNA adduct production.[27] Other studies report no increased chromosomal changes in the body fluids of nonsmokers exposed to ETS.[28-29]

Toxicity (Sidestream Smoke)

Animal inhalation experiments using fresh sidestream smoke or constituents of sidestream smoke fail to support the claim

2023469057

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

that ETS is a pulmonary carcinogen. Two such experiments have been published; both reportedly found no meaningful differences in the lung tissue of animals exposed to sidestream smoke and those not exposed to the smoke. In one of the studies, German scientists exposed rats and hamsters to very high levels of sidestream smoke for a 90-day period; they reported no significant physiological effects on the tissues of the animals.[30] In the second study, researchers from the American Health Foundation exposed hamsters to sidestream and mainstream smoke for 18 months; they observed no significant increase in lung tumors among the animals exposed to sidestream smoke.[31-33]

In addition, recent reviews of the literature on suspected pulmonary carcinogens have concluded that none of the individual constituents in sidestream smoke which are classified as potentially carcinogenic have been found to induce pulmonary cancer via inhalation in experimental animals.[34-35]

Constituents of ETS

A number of constituents typically have been cited in the literature to demonstrate the contribution of ETS to the indoor air. These include carbon monoxide, particulates, nicotine, and nitrosamines. However, the use of one or any combination of such constituents to determine ETS levels presents many problems. For

2023469058

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

example, although analytic and sampling methods continue to improve, there is at present no completely satisfactory and uniform procedure for measuring ETS.[36-37] Moreover, although the reported findings of studies which measure constituents in experimental conditions (e.g., in unventilated smog chambers) are frequently cited to dramatize the potential effect of ETS on indoor air, they have little, if any, similarity to those of studies which measure ETS in realistic settings. And finally, with the exception of nicotine, none of the constituents which have been used as substitute measures for ETS are characteristic of ETS alone. Other sources, such as heaters, stoves and furnishings, generate greater levels of those substances than those found in ETS.[38-40]

Exposure to ETS

Published studies indicate that nonsmoker exposure to ETS constituents under normal, everyday conditions is minimal. For example, researchers report that there is little difference in ambient levels of carbon monoxide (CO) in smoking and nonsmoking areas of workplaces and other public places and in homes with and without smokers.[12,15,38,41-44] Other studies indicate that ETS contributes less than half of the total particles in the air of an average public place.[2,13-15,45-49] Typical measurements of nicotine, which is used as a marker for ETS exposures because it is unique to tobacco smoke, range from an exposure equivalent of one

2023469059

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

one-hundredth (1/100) to less than one one-thousandth (1/1000) of a filter cigarette per hour.[13-16,50-56] This means that a nonsmoker would have to spend from 100 to 1,000 hours in an office, restaurant or other public place where smoking is permitted in order to be exposed to the nicotine equivalent of a single cigarette.

Carbon Monoxide

Research has shown that the main sources of CO in the outdoor urban environment are motor vehicles and industrial processes,[57] and that indoor levels are affected by these outdoor sources, mainly through ventilation, and by numerous activities such as cooking and heating. In fact, studies have indicated that gas stoves in kitchens and heating units are often major sources of CO in homes.[38,58-59]

After their review of such studies, participants at the University of Geneva symposium on ETS in 1983 concluded that CO from environmental tobacco smoke "is not important from a health point of view."[60] Similarly, researchers from the Lawrence Berkeley Laboratory in the U.S., who are otherwise critical of tobacco smoke, concluded that "based on theoretical and empirical results, CO sidestream emissions from cigarettes have often been overemphasized."[42]

2023469060

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Particulates

A paper published in a 1980 issue of Science magazine, in which the authors reported the results of their efforts to measure particles or particulates in the air of smoking and nonsmoking areas, is often cited to support the claim that ETS is a major indoor pollutant.[61] The authors, Repace and Lowrey, contend that the levels of particles they observed in smoking areas were much higher than in the nonsmoking areas. However, their study results are inconsistent with many others. For example, the average particle count attributed to ETS in their study was from three to more than 20 times higher than the average levels reported in other studies of office buildings, restaurants and residences.[2,13-15,48,62-64]

There are a number of explanations for Repace/Lowrey's apparent overestimation of ETS exposure. First, they selectively sampled environments such as meeting and game rooms, bars and sandwich shops which do not represent normal occupancy conditions and where particulate levels are likely be high regardless of the presence or absence of tobacco smoke. Second, through inappropriate testing methods, they incorrectly assumed that all particles in the air arose from ETS. However, as several researchers have noted, ETS typically contributes less than half of the overall particle levels reported in indoor spaces,[45-47]

2023469061

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

perhaps because particles are also generated by people and their everyday routine activities such as movement and cooking.[65-66]

In addition to ignoring potential indoor sources of particles, the study has been criticized on other grounds. For example, Repace and Lowrey did not measure ventilation rates or humidity, and they failed to clean and calibrate their testing instrument prior to making their measurements.[66] Indeed, the testing device they used "is no longer recommended" for measuring tobacco smoke.[36-37]

In their report, Repace and Lowrey implied that the particle levels attributed to ETS are potentially harmful to the health of nonsmokers. However, an earlier study by Bouhuys, et al., reportedly found "no evidence that high TSP (total suspended particulates) levels in homes with smokers were associated with increased symptoms or lung function loss among nonsmokers in the same home."[67] Binder, et al., also reported that respirable particulate levels in homes were "independent of the presence or absence of respiratory disease."[68] More recently, Lebowitz, et al., reported on data which showed that respiratory symptoms in asthmatics were associated with total indoor particle levels (e.g., dust), but not with the presence of tobacco smoke.[63,69-70]

2023469062

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Particulates and Radon

A theory suggesting that concentrations of radon decay products increase in the presence of tobacco smoke, thus implying an increased risk of lung cancer for nonsmokers, has been reported in the literature.[71-73] The theory suggests that radon decay products attach to particles (including ETS) in the air, remain suspended, and are subsequently taken up in the lungs of nonsmokers. However, data from actual research studies indicate that it is the unattached, gaseous fraction of radon which determines the amount of radiation to which the respiratory tract is exposed.[74-76] According to these data, the unattached fraction of radon daughters will decrease as dust or particulate levels increase, thereby lowering the potential dose of radiation to the lungs.

Nicotine

Since ambient nicotine is produced almost exclusively by burning tobacco, it is considered to be a more reliable indicator of the amount of tobacco smoke in the environment than other smoke constituents. Studies which have used nicotine in this way suggest that tobacco smoke contributes very little to the indoor atmosphere.[12-16,50-56] For example, Drs. William Hinds and Melvin First of the Harvard School of Public Health reportedly found very small

2023469063

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

amounts of nicotine in the atmospheres of bars, bus and airline terminals, restaurants, and cocktail and student lounges.[50] French researchers, using a different method of measuring nicotine to assess the amount of tobacco smoke in the atmosphere, reported finding higher concentrations of nicotine than Hinds and First.[51] However, they still concluded that "smoking does not present a risk to nonsmokers."

Other studies have reached similar conclusions. In 1984, Japanese researchers tested a personal nicotine monitor in a number of public places, including offices, restaurants, lobbies, terminals and public transportation. They reported levels of nicotine exposure equivalent to one one-thousandth (1/1000) to four one-hundredths (4/100) of a cigarette per hour.[53] Their findings were repeated in 1987.[54]

A year later, scientists from IT Corporation, a firm specializing in the assessment and reduction of environmental substances, measured nicotine in offices and restaurants in Ottawa, Canada.[13] They reported average nicotine exposure levels equivalent to three one-hundredths (3/100) of a cigarette per eight-hour workday, and three one-thousandths (3/1000) of a cigarette during a one-hour meal.

2023469064

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In a nationwide sampling survey in the United Kingdom, researchers monitored nearly 3,000 sites in travel, work, home and leisure locations for ambient nicotine, CO and particle levels.[12] Smoking was known to have occurred at almost half of those sites, yet in three-fourths of the samples, nicotine levels were too low to be detected. Canadian researchers also reported levels of nicotine at or below levels of detection even in locations with recirculated air from designated smoking areas.[64]

There are few data that suggest that the tiny amounts of nicotine to which a nonsmoker may be exposed are related to human disease. For example, two German scientists monitored several physiological responses in nonsmokers exposed to tobacco smoke under laboratory conditions.[78] They concluded that the amount of nicotine to which their subjects were exposed was too small to alter sensitive test measurements of heart rate, heart muscle tracings (EKG), blood pressure or skin temperature. More recent research tends to support these conclusions. In a 1983 study, researchers who measured exposures of nonsmoking flight attendants to nicotine during transpacific flights concluded that the concentrations were so small that they were "unlikely to have physiologic effects."[56] In 1986, researchers monitored levels of nicotine, CO and particulates in 66 commercial flights in the U.S. They concluded that the non-smoking sections of commercial aircraft were essentially free of ETS.[16]

2023469065

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Other Constituents

Studies which have examined levels of nitrosamines, nitrogen oxides and volatile organic compounds (such as benzene) in ETS report that it makes minimal contributions to overall ambient air levels in homes, the workplace and public places.[38-40,48,79-88] However, this has not prevented claims from being made that such exposures are harmful to the nonsmoker.

For example, it has been claimed, largely on the basis of reports by Brunnemann, et al., that nitrosamines from tobacco smoke represent a cancer risk to nonsmokers.[89-90] It has also been claimed that nitrosamine levels in sidestream smoke exceed those found in mainstream smoke, with the implication that those levels are also found in ETS. However, this is not the case. In 1982, Austrian scientists reported that their measurements of nitrosamine levels in ordinary public places were far below the values reported earlier by Brunnemann and his co-workers. They emphasized that the levels of nitrosamines which may occur in environmental tobacco smoke "are quite different" from those found in sidestream smoke.[80]

One scientist who reviewed the literature stated that nitrosamines occur everywhere "independent of any type of tobacco

2023469066

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

combustion, in which case concentrations are often reached in respiratory air that are far above those that may be produced by tobacco smoke."[91] He concluded that, as a consequence, any claimed implications of health risks from nitrosamines in tobacco smoke "clearly move into the range of speculation." Another scientist, Dr. Helmut Schievelbein, Director of the Institute of Clinical Chemistry in Munich, Germany, observed that concentrations of nitrosamines either consumed or generated daily by individuals are "many times greater" than those found in environmental tobacco smoke.[79]

Other constituents which have been identified in analyses of sidestream smoke are often assumed to contribute substantially to indoor air in the form of ETS. The most commonly mentioned constituents include nitrogen dioxide (NO_2), formaldehyde and volatile organic compounds. However, these compounds are present in very small amounts in ETS.[39-40,48] Recent studies report no correlations between ETS and levels of NO_2 and volatile organic compounds in residences and offices.[39,48,83-84] Indeed, research indicates that levels of these components generated from other ordinary sources (e.g., cooking stoves, heaters and building materials) are much greater than those contributed by cigarette smoking.[39,83-84]

2023469067

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Reports have also suggested that exposure to benzene from ETS is substantial.[92-93] However, a recent study by German investigators reported that benzene uptake by nonsmokers exposed to ETS is negligible compared to background levels from other environmental sources.[85] Other scientists, who compared benzene emissions from cigarettes with those reported from automobiles, have observed that "an average person is potentially exposed to 1,000 times more ambient benzene from one automobile than from a smoker in a given year."[94]

Cotinine as a Marker for ETS Exposures

It has been reported that cotinine, a substance metabolized or converted from nicotine by the body, can be used as a biological marker to measure nonsmoker exposure to ETS.[95-96] While some reports suggest that cotinine is a reliable marker for total exposure to tobacco smoke, many others do not for a variety of reasons.[97-106] For example, it has been reported that individuals metabolize nicotine in different ways at different times and that elimination rates for cotinine vary among individuals. In addition, recent research indicates that diet may contribute to levels of nicotine and cotinine found in the body, thereby interfering with reported exposure levels from nicotine in the ambient air.[107] Scientists have also noted that different methods of analysis may influence final recorded levels of

2023469068

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

cotinine.[108] And finally, it has been observed that because nicotine is largely present in the gas-phase of ETS, measurement levels of its metabolite, cotinine, do not reflect exposures to other constituents present, for example, in the particulate phase of ETS.[99]

For these reasons, cotinine should not be regarded as a reliable quantitative measure of ETS exposure. At best, cotinine may be used as a qualitative marker of ambient nicotine exposures.

Other Determinations of ETS Exposure/Thresholds

Despite the difficulties researchers have encountered in determining ETS exposure, it has been suggested that the nonsmoker's risk of disease attributable to ETS can be estimated by comparing the levels of exposure to ETS with the active smoker's exposure to mainstream smoke. These estimates are derived by extrapolating the exposure (and, thus, the imputed risks) of active smoking to nonsmoker exposure to ETS. However, such an extrapolation is based upon several unwarranted assumptions.[109] First, it assumes that mainstream smoke and ETS are chemically and physically comparable. The foregoing discussion demonstrates that this is not the case. Indeed, even the 1986 Report of the Surgeon General on ETS conceded:

2023469069

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

> Comparison of the relative concentrations of various components of SS and MS smoke provides limited insights concerning the toxicological potential of ETS in comparison with active smoking. . . . SS characteristics, as measured in a chamber, do not represent those of ETS, as inhaled by the nonsmoker under nonexperimental conditions.[110]

Similarly, the 1986 NAS Report on ETS concluded:

> Because the physicochemical nature of ETS, MS, and SS differ, the extrapolation of health effects from studies of MS or of active smokers to nonsmokers exposed to ETS may not be appropriate . . . .[111]

Second, it assumes the validity of a "linear extrapolation" from active smoking to nonsmoker exposure to ETS. That is, it assumes that the level of exposure to active smoking (and the implied risk) for the smoker can be utilized to calculate the implied risk of the nonsmoker on the basis of his proportionate exposure to ETS. This model, however, has never been verified experimentally, nor has it been demonstrated to be applicable to ETS or its constituents.[112]

In fact, dose-extrapolation models which are based upon realistic estimates of exposure and dose for nonsmokers fail to predict an appreciable increased risk of disease for nonsmokers exposed to ETS.[113-114,116] It has been estimated, for example, that a nonsmoker is exposed to approximately two-hundredths of one

2023469070

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

percent (0.02%) of the particulates to which an active smoker is exposed.[11,109,113-115] Consequently, the reported risk estimates are typically many times lower than risk estimates which are based upon the epidemiologic or population-based studies of ETS. These two different methods of risk assessment lead to markedly incompatible results. Indeed, the Project Officer for the EPA's draft risk assessment on ETS revealed that the drafters of the report were "unsuccessful" in their attempts to estimate a dose-response relationship by extrapolating from active smoking (mainstream smoke) to ETS exposure, and that, as a result, they decided to "present other methods" to estimate the risk of disease from ETS exposure.[117]

Summary

A review of the published literature on ETS demonstrates that exposure to ETS in typical indoor environments is minimal. Yet tobacco smoke, because it is visible, has become a target for those who apparently want a quick, simple solution to the problem of indoor air pollution. However, as one Canadian scientist observed, "the claim that smoking is responsible for indoor air pollution is an oversimplification of a complex, multi-source problem."[66]

2023469071

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

ENVIRONMENTAL TOBACCO SMOKE AND INDOOR AIR QUALITY

1. Sterling, T., et al., "Indoor Byproduct Levels of Tobacco Smoke: A Critical Review of the Literature," J Air Pollut Control Assoc 32(3): 250-259, 1982.

2. Sterling, T., et al., "Environmental Tobacco Smoke and Indoor Air Quality in Modern Office Work Environments," J Occup Med 29(1): 57-62, 1987.

3. Pedelty, J. and Holcomb, L., "A Computer Simulation of Indoor Air Quality Which Models Changes in Point Sources and Ventilation," Environ Technol Letters 11: 1053-1062, 1990.

4. Baker, R., et al., "The Origins and Properties of Environmental Tobacco Smoke," Env Int (16): 231-245, 1990.

5. Scherer, G., et al., "Importance of Exposure to Gaseous and Particulate Phase Components of Tobacco Smoke in Active and Passive Smokers," Occup Env Health (62): 459-466, 1990.

6. Rawbone, R., "The Aging of Sidestream Tobacco Smoke Components in Ambient Environments." In: Indoor Air Quality. H. Kusuga (ed.). Berlin, Heidelberg, Springer-Verlag, 55-61, 1990.

7. Proctor, C., et al., "The Measurement of ETS Through Adsorption/Desorption Procedures." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 82-89, 1990.

8. Piade, J., et al., "Assessment of ETS Impact on Office Air Quality." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 112-119, 1990.

9. Löfroth, G., et al., "Characterization of Environmental Tobacco Smoke," Env Sci Technol (23): 610-614, 1989.

10. Nystrom, C., et al., "Assessing the Impact of Environmental Tobacco Smoke on Indoor Air Quality: Current Status." In: Proceedings of the ASHRAE Conference, IAQ '86: Managing Indoor Air for Health and Energy Conservation, Atlanta, Georgia, 213-233, April 20-23, 1986.

11. Adlkofer, F. "Biological Effects After Exposure to ETS." In: Indoor Air Quality. Buenos Aires, The National Academy of Sciences of Buenos Aires, 61-78, 1989.

2023469072

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

12. Kirk, P., et al., "Environmental Tobacco Smoke in Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 99-112, 1988.

13. Carson, J. and Erikson, C., "Results from Survey of Environmental Tobacco Smoke in Offices in Ottawa, Ontario," Environ Technol Letters 9: 501-508, 1988.

14. Oldaker, G., et al., "Results From Surveys of Environmental Tobacco Smoke in Restaurants." In: Indoor Air Quality, H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 99-104, 1990.

15. Sterling, T. and Mueller, B., "Concentrations of Nicotine, RSP, CO and CO_2 in Nonsmoking Areas of Offices Ventilated by Air Recirculated from Smoking Designated Areas," Am Ind Hyg Assoc J 49(9): 423-426, 1988.

16. Oldaker, G. and Conrad, F., "Estimation of the Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft," Environ Sci Technol 21: 994-999, 1987.

17. Bos, R., et al., "Excretion of Mutagens in Human Urine After Passive Smoking," Cancer Letters (19): 85-90, 1983.

18. Husgafvel-Pursiainen, K., et al., "Passive Smoking at Work: Biochemical and Biological Measures of Exposure to Environmental Tobacco Smoke," Int Arch Occup Environ Health (59): 337-345, 1987.

19. Mohtashamipur, E., et al., "Urinary Excretion of Mutagens in Passive Smokers," Toxicology Letters (35): 141-146, 1987.

20. Scherer, G., et al., "Urinary Mutagenicity After Controlled Exposure to Environmental Tobacco Smoke (ETS)," Toxicology Letters 35(1): 135-140, 1987.

21. Bombick, D., et al., "Assessment of the Biological Activity of Mainstream or Environmental Tobacco Smoke (ETS) Using a Cellular Smoke Exposure Technique," Abstracts of the Twenty-Second Annual Scientific Meeting of the Environmental Mutagen Society, Kissimmee, Florida, April 6-11, 1991.

22. Scherer, G., "Biomonitoring of Exposure to Potentially Genotoxic Substances From Environmental Tobacco Smoke," Environ Int (15): 49-56, 1989.

23. Scherer, G., "Quantitative and Qualitative Differences in Tobacco Smoke Uptake Between Active and Passive Smoking."

2023469073

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 189-194, 1988.

24. Scherer, G., et al., "Urinary Mutagenic, Hydroxy-Phenanthrene, and Thioether Excretion After Exposure to Environmental Tobacco Smoke." In: Indoor Air Quality, H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 138-146, 1990.

25. Martin, F., et al., "Urinary Excretion of Hydroxy-Phenanthrenes After Intake of Polycyclic Aromatic Hydrocarbons," Environ Int (15): 41-47, 1989.

26. Hoepfner, H., et al., "Hydroxy-Phenanthrenes in the Urine of Non-Smokers and Smokers," Toxicology Letters (35): 67-71, 1987.

27. Holz, O., et al., "^{32}P-postlabelling Analysis of DNA Adducts in Monocytes of Smokers and Passive Smokers," Int Arch Occup Environ Health, 62: 299-303, 1990.

28. Sorsa, M., et al., "Cytogenetic Effects of Tobacco Smoke Exposure Among Involuntary Smokers," Mutation Res 222(2): 111-116, 1989.

29. Husgafvel-Pursiainen, K., "Sister-Chromatid Exchange and Cell Proliferation in Cultured Lymphocytes of Passively and Actively Smoking Restaurant Personnel," Mutation Res 190: 211-215, 1987.

30. Adlkofer, F., et al., "Exposure of Hamsters and Rats to Sidestream Smoke of Cigarettes: Preliminary Results of a 90-Day-Inhalation Study." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 252-258, 1988.

31. Haley, N., et al., "Uptake of Sidestream Smoke by Syrian Golden Hamsters," Toxicol Letters 35: 83-88, 1987.

32. Haley, N., "Sidestream Smoke Uptake By Syrian Golden Hamsters in an Inhalation Bioassay," Indoor Air '87: Proceedings of the 4th International Conference on Indoor Air Quality and Climate, Berlin, Volume 2, 68-73, August 17-21, 1987.

33. Hoffmann, D., American Health Foundation, "Experimental Tobacco Carcinogenesis: 2 PO1 CA29580-07, Subproject 6: Sidestream Smoke Carcinogenesis," Application for Continuation Grant to U.S. Department of Health and Human Services, Public Health Service, April 29, 1988.

2023469074

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

34. Aviado, D., "Suspected Pulmonary Carcinogens in Environmental Tobacco Smoke," Environ Tech Letters, 9: 539-544, 1988.

35. Aviado, D., "Health Effects of 50 Selected Constituents of Environmental Tobacco Smoke." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 383-389, 1990.

36. First, M., "Environmental Tobacco Smoke Measurements: Retrospect and Prospect." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement 133, Vol. 65, 9-16, 1984.

37. Jenkins, R. and Guerin, M., "Analytical Chemical Methods for the Detection of Environmental Tobacco Smoke Constituents." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement 133, Vol. 65, 33-46, 1984.

38. Cox, B. and Whichelow, M., "Carbon Monoxide Levels in the Breath of Smokers and Nonsmokers: Effect of Domestic Heating Systems," J Epidemiol Community Health 39: 75-78, 1985.

39. Good, B., et al., "Effect of Cigarette Smoking on Residential NO_2 Levels," Environ Int 8: 167-175, 1982.

40. Godish, T., "Formaldehyde Exposures from Tobacco Smoke: A Review," AJPH 79(8): 1044-1045, 1989.

41. Duncan, D. and Greavey, P., "Passive Smoking and Uptake of Carbon Monoxide in Flight Attendants," JAMA 251(20): 120-121, 1984.

42. Girman, J. and Traynor, G., "Indoor Concentrations," J Air Pollut Control Assoc, 33(2): 89, 1983.

43. Yocom, J., "Indoor Concentrations," J Air Pollut Control Assoc, 33(2): 89, 1983.

44. Nitta, H., et al., "Measurements of Indoor Carbon Monoxide Levels Using Passive Samplers in Korea," Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 77-82, July 29-August 3, 1990.

2023469075

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

45. Ogden, M. and Maiolo, K., "Collection and Analysis of Solanesol as a Tracer of Environmental Tobacco Smoke (ETS)." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 77-88, 1988.

46. Proctor, C., "The Analysis of the Contribution of ETS to Indoor Air." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 57-66, 1988.

47. Eatough, D., et al., "Assessing Exposure to Environmental Tobacco Smoke." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 131-140, 1988.

48. Proctor, C., et al., "Measurements of Environmental Tobacco Smoke in an Air-Conditioned Office Building," Environ Technol Letters (10): 1003-1018, 1989.

49. Proctor, C., "A Multi-Analyte Approach to the Measurement of Environmental Tobacco Smoke." In: Indoor Air Quality and Ventilation. F. Lunau and G. Reynolds (eds.). London, Selper Ltd, 427-436, 1990.

50. Hinds, W. and First, M., "Concentrations of Nicotine and Tobacco Smoke in Public Places," New Eng J Med 292(16): 844-845, 1975.

51. Badre, R., et al., "Pollution Atmospherique par la Fumee de Tabac (Atmospheric Pollution by Smoking)," Ann Pharm Fr 36(9-10): 443-452, 1978. Translation.

52. Jenkins, R., et al., "Development and Application of a Thermal Desorption-Based Method for the Determination of Nicotine in Indoor Environments." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 557-566, 1988.

53. Muramatsu, M., et al., "Estimation of Personal Exposure to Tobacco Smoke with a Newly Developed Nicotine Personal monitor," Environ Res 35: 218-227, 1984.

54. Muramatsu, M., et al., "Estimation of Personal Exposure to Ambient Nicotine in Daily Environment," Arch Occup Environ Health 59: 545-550, 1987.

55. Thompson, C., et al., "A Thermal Desorption Method for the Determination of Nicotine in Indoor Environments," Environ Sci Technol 23: 429-435, 1989.

56. Foliart, D., et al., "Passive Absorption of Nicotine in Airline Flight Attendants," New Eng J Med 308(18): 1105, 1983.

2023469076

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

57. Stewart, R., "The Effects of Low Concentrations of Carbon Monoxide in Man." In: Environmental Tobacco Smoke Effects on the Nonsmoker: Report from a Workshop. R. Rylander (ed.). Published in Scand J Respir Dis, Suppl. 91: 56-62, 1974.

58. Wade, W., "A Study of Indoor Air Quality," J Air Pollut Control Assoc 25(9): 933-939, 1975.

59. Yocom, J., "Indoor-Outdoor Air Quality Relationships," J Air Pollut Control Assoc 32(5): 500-520, 1982.

60. Rylander, R., "Workshop Perspectives." In: ETS-Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement 133, Vol. 65, 143-145, 1984.

61. Repace, J. and A. Lowrey, "Indoor Air Pollution, Tobacco Smoke and Public Health," Science 208: 464-472, 1980.

62. Hosein, R., "The Relationship Between Pollutant Levels in Homes and Potential Sources." In: Transactions: Indoor Air Quality in Cold Climates, Hazards and Abatement Measures. D. Walkinshaw (ed.). Pittsburgh, Air Pollution Control Association, 250-260, 1986.

63. Quackenboss, J. and Lebowitz, M., "Indoor-Outdoor Relationships for Particulate Matter: Exposure Classifications and Health Effects," Environ Int 15: 353-360, 1989.

64. Sterling, T., "ETS Concentrations Under Different Conditions of Ventilation and Smoking Regulation." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 89-98, 1988.

65. First, M., "Constituents of Sidestream and Mainstream Tobacco Smoke and Markers to Quantify Exposure to Them." In: Indoor Air and Human Health. Chelsea, Michigan, Lewis Publishers, 195-203, 1985.

66. Sterling, T., "Discussion -- Tobacco Smoke, Ventilation, and Indoor Air Quality," ASHRAE Transactions 88(1): 911-912, 1982.

67. Bouhuys, A., et al., "Do Present Levels of Air Pollution Outdoors Affect Respiratory Health?," Nature 276: 466-471, 1978.

2023469077

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

68. Binder, R., et al., "Importance of the Indoor Environment in Air Pollution Exposure," Arch Environ Health 31(6): 277-279, 1976.

69. Lebowitz, M., et al., "Respiratory Symptoms and Peak Flow Associated with Indoor and Outdoor Air Pollutants in the Southwest," J Air Pollut Control Assoc 35: 1154-1158, 1985.

70. Lebowitz, M., "The Effects of Environmental Tobacco Smoke Exposure and Gas Stoves on Daily Peak Flow Rates in Asthmatic and Non-Asthmatic Families." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement 133, Vol. 65, 90-97, 1984.

71. Bergman, H. and Axelson, O., "Passive Smoking and Indoor Radon Daughter Concentrations," Lancet: 1308-09, 1983.

72. Bergman, H., et al., "Indoor Radon Daughter Concentrations and Passive Smoking," Env Int (12): 17-19, 1986.

73. Moghissi, A. and Seiler, M., "Enhancement of Exposure to Radon Progeny as a Consequence of Passive Smoking," Env Int (15): 261-64, 1989.

74. Upfal, M., et al., "Indoor Radon and Lung Cancer in China," J of the National Cancer Inst: 1722, 1989.

75. Stebbings, J. and Dignam, J., "Contamination of Individuals by Radon Daughters: A Preliminary Study," Archives of Environ Health 43(2): 149-54, 1988.

76. Pritchard, J. and Strong, J., "The Influence of Environmental Tobacco Smoke on Radon Dosimetery." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 3, 33-38, July 29-August 3, 1990.

77. McAughey, J., et al., "Risk Assessment of Exposure to Indoor Air Pollutants," Env Int (11): 295-302, 1990.

78. Harke, H. and Bleichert, A., "Zum Problem des Passivrauchens (On the Problem of Passive Smoking)," Int Arch Arbeitsmed 29: 312-333, 1972. Translation.

79. Schievelbein, H., "Are There Really Important New Findings About Passive Smoking?," Oeff Gesundheitswes 44: 454-456, 1982. Translation.

2023469078

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

80. Stehlik, G., et al., "Concentration of Dimethylnitrosamine in the Air of Smoke-Filled Rooms," Ecotoxicol Environ Safety 6: 495-500, 1982.

81. Sega, K. and Fugas, M., "Nitrogen Dioxide Concentrations in Residences." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 493-496, 1988.

82. Shimizu, Y., et al., "Influence of Indoor Air Pollution on NO_2 Personal Exposure Levels of Schoolchildren." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Brussels, Elsevier Science Publishers, 337-345, 1989.

83. Hendel-Kramer, A., et al., "Regression Model for Indoor Concentrations of Combustion-Generated Gases." In: Present and Future of Indoor Air Quality. C. Bieva, et al. (eds.). Brussels, Elsevier Science Publishers, 315-320, 1989.

84. Bayer, C. and Black, M., "Thermal Desorption/Gas Chromatographic/Mass spectrometric Analysis of Volatile Organic Compounds in the Offices of Smokers and Nonsmokers," Biomed and Envir Mass Spect 14(8): 363-367, 1987.

85. Adlkofer, F., et al., "Significance of Exposure to Benzene and Other Toxic Compounds Through Environmental Tobacco Smoke," J Cancer Res Clin Oncol (116): 591-598, 1990.

86. Godish, T., "Residential Formaldehyde: Increased Exposure Levels Aggravate Adverse Health Effects," J of Environ Health 53(3): 34-35, 1990.

87. Hugod, C., et al., "Exposure of Passive Smokers to Tobacco Smoke Constituents," Int Arch Occup Environ Health (42): 21-29, 1978.

88. Proctor, C., et al., "Measurement of Environmental Tobacco Smoke in an Air-Conditioned Office Building." In: Present and Future of Indoor Air Quality. C.J. Bieva, et al. (eds.). Brussels, Elsevier Science Publishers, 169-172, 1989.

89. Brunnemann, K., et al., "Assessment of Carcinogenic Volatile N-Nitrosamines in Tobacco and in Mainstream and Sidestream Smoke from Cigarettes," Cancer Res 37: 3218-3222, 1977.

90. Brunnemann, K. and D. Hoffmann, "Chemical Studies on Tobacco Smoke. LIX. Analysis of Volatile Nitrosamines in Tobacco Smoke and Polluted Indoor Environments." In: Environmental Aspects of N-Nitroso Compounds. E. A. Walker, et al. (eds.). Lyon, IARC Scientific Publications, 343-355, 1978.

2023469079

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

91. Lehnert, G., "Schlusswort: Zum Bereich des Spekulativen (Conclusion: In the Realm of Speculation)," Münch Med Wschr 124(4): 19-20, 1982. Translation.

92. Hattemer-Frey, H., "Benzene: Environmental Partitioning and Human Exposure," Environ Res 53: 221-232, 1990.

93. Wallace, L., "Major Sources of Exposure to Benzene and Other Volatile Organic Chemicals," Risk Analysis 10(1): 59-64, 1990.

94. R.J. Reynolds Tobacco Company, "Response" to the U.S. Environmental Protection Agency's Environmental Tobacco Smoke: A Guide to Workplace Smoking Policies," Public Review Draft, EPA/400/6-90/004, Volume 1, 32, October 1, 1990.

95. Wald, N., et al., "Urinary Cotinine as Marker of Breathing Other People's Tobacco Smoke," Lancet I: 230-231, 1984.

96. Watts, R., et al., "Cotinine Analytical Workshop Report: Consideration of Analytical Methods for Determining Cotinine in Human Body Fluids as a Measure of Passive Exposure to Tobacco Smoke," Environ Health Persp 84: 173-182, 1990.

97. Curvall, M., et al., "Simulation and Evaluation of Nicotine Intake During Passive Smoking: Cotinine Measurements in Body Fluids of Nonsmokers Given Intravenous Infusions of Nicotine," Clin Pharmacol Ther 47(1): 42-49, 1990.

98. Itani, S., et al., "A Comparison of Plasma and Urinary Nicotine and Cotinine Levels in Smokers and Nonsmokers: Nicotine Excretion Pathways are Possibly Differential According to the Dosage of Tobacco Smoke Uptake." In: Indoor Air Quality. H. Kasuga (ed.). Berlin, Heidelberg, Springer-Verlag, 202-212, 1990.

99. Idle, J., "Commentary: Titrating Exposure to Tobacco Smoke Using Cotinine -- A Minefield of Misunderstanding," J Clin Epidemiol 43(4): 313-317, 1990.

100. Biber, A., et al., "Determination of Nicotine and Cotinine in Human Serum and Urine: An Interlaboratory Study," Toxicology Letters 35(1): 45-52, 1987.

101. Haley, N., et al., "Elimination of Cotinine from Body Fluids: Disposition in Smokers and Nonsmokers," AJPH 79(8): 1046-1048, 1989.

2023469080

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

102. Cummings, K., et al., "Measurement of Current Exposure to Environmental Tobacco Smoke," Archives of Environ Health 45(2): 74-79, 1990.

103. Lee, P., "Lung Cancer and Passive Smoking," Br J Cancer 63: 161-162, 1991.

104. Johnson, L., et al., "Passive Smoking Under Controlled Conditions," Int Arch Occup Environ Health 56: 99-110, 1985.

105. Letzel, H., et al., "Measuring Problems in Estimating the Exposure to Passive Smoking Using the Excretion of Cotinine," Toxicology Letters 35(1): 35-44, 1987.

106. Schwartz, S., et al., "Mathematical Modelling of Nicotine and Cotinine as Biological Markers of Environmental Tobacco Smoke Exposure," Toxicology Letters 35(1): 53-58, 1987.

107. Castro, A. and Monji, N., "Dietary Nicotine and Its Significance in Studies on Tobacco Smoking," Bio Arch 2(2): 9197, 1986.

108. Adlkofer, F., et al., "Passive Smoking," N Engl J Med 312(11): 719-720, 1984.

109. Reasor, M. and Will, J., "Assessing Exposure to Environmental Tobacco Smoke: Is it Valid to Extrapolate from Active Smoking?," J Smoking-Related Dis 2(1): 111-127, 1991.

110. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

111. Committee on Passive Smoking, Board on Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects, Washington, D.C., National Academy Press, 1986.

112. Rüdiger, H., "Carcinogens: Requiring a New Yardstick," Hamburger Arzteblatt: 207, June 1989. Translation.

113. Arundel, A., et al., "Never Smoker Lung Cancer Risks from Exposure to Particulate Tobacco Smoke," Environ Int 13: 409-426, 1987.

114. McAughey, J., et al., "Respiratory Deposition of Environmental Tobacco Smoke." In: Indoor Air '90: Proceedings of the

2023469081

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 2, 361-366, July 29-August 3, 1990.

115. R.J. Reynolds Tobacco Company, "Comments" on Appendix C, "Dosimetry of Environmental Tobacco Smoke," Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA/600/6-90/006A, B1-B25, October 1, 1990.

116. Darby, S. and Pike, M., "Lung Cancer and Passive Smoking: Predicted Effects from a Mathematical Model for Cigarette Smoking and Lung Cancer," Br J Cancer 58: 825-831, 1988.

117. Bayard, S., Statement, The U.S. Enviromental Protection Agency Science Advisory Board Hearing on Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA/600/6-90/006A, 116-117, December 4, 1990. Transcript.

2023469082

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

IV. ENVIRONMENTAL TOBACCO SMOKE AND THE PUBLIC

> There is a new segment emerging in our society -- that of the social engineer, bureaucratic wowser, or health fanatic. A group of people who are attempting to enforce their beliefs on a community which has the right to choose what to eat, drink and smoke.[1]

Exposure to environmental tobacco smoke under extreme conditions may provoke complaints of irritation and annoyance. However, the mere sight and smell of tobacco smoke may be enough to produce strong reactions in individuals who intensely dislike smoking. Although the extent to which environmental tobacco smoke may bother or annoy individuals under normal conditions has not been established scientifically, it has been suggested that extreme reactions to tobacco smoke exposure may have a strong emotional or psychological basis.[2-4] Whatever the reasons for such reactions, the literature on this subject suggests it is misleading to claim, as antismokers frequently do, that such subjective or emotional reactions have a physical basis.

Governmental Regulations and Individual Rights

Although antismoking organizations claim to seek protection for the health and welfare of the nonsmoker, their efforts to make smoking socially unacceptable are part of a broader objective -- the severe restriction or even prohibition of smoking by

2023469083

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

governmental legislation. Of course, such regulations restrict the freedom of the smoker, and antismokers are compelled to justify this kind of political control of individual behavior. They have accomplished this, in large measure, by exploitation of the so-called "health" argument involving ETS exposures to nonsmokers.

For example, the 1986 U.S. Surgeon General's Report contends that ETS causes lung cancer in adult nonsmokers and respiratory conditions in children, and that the separation of smokers and nonsmokers is not an effective method of minimizing the nonsmoker's exposure to ETS.[5] The Report concludes that smoking bans will not only reduce ETS exposures, but will also "alter smoking behavior and public attitudes about tobacco use." The Report further suggests that "over time, this may contribute to a reduction of smoking." Thus, the underlying motivation for the use of the ETS/health argument is to attain a "smoke-free society by the year 2000."

The Surgeon General's tactics, however, have been questioned by a number of critics. One reviewer suggested that the Surgeon General's conclusions were based on "flimsy" evidence presented in an effort to "divert attention" from important health concerns such as the "poisoning of the environment."[6] A U.S. Congressman, in a letter to the Congressional Record, wrote that "the conclusions in the Surgeon General's Report are not supported

2023469084

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

by the research in his own report."[7]

Moreover, the Surgeon General's claim that separation of smokers and nonsmokers does not minimize nonsmoker exposure to ETS is without scientific support. Studies aboard commercial aircraft and in offices indicate, contrary to the Surgeon General's Report, that the simple separation of smokers and nonsmokers effectively minimizes nonsmoker exposure to ETS.[8-16] One recent study, for example, reported that the use of designated smoking areas reduced exposure to ETS by 95 percent.[8] Another study of a smoking-restricted office building reported that ambient nicotine in nonsmoking areas was virtually undetectable, suggesting that ETS had a negligible impact on the nonsmoking areas in the building.[9] In addition, Canadian researchers, in a series of studies, collected data on levels of ETS constituents in offices with different smoking regulations. They reported no significant differences in average ETS constituent levels between nonsmoking offices that received recirculated air from designated smoking areas and nonsmoking offices that did not receive recirculated air.[10-11,14,16] They concluded:

> The results indicate that the provision of a designated, but not separately ventilated smoking area can effectively eliminate or drastically reduce most components of environmental tobacco smoke from nonsmoking offices.

2023469085

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Similarly, restrictions and bans on smoking aboard commercial aircraft have been imposed despite the availability of data suggesting that the simple separation of smokers and nonsmokers effectively reduces exposure to ETS. A case in point was the 1989 decision by the United States Congress to ban smoking aboard flights of six hours or less. This Congressional action was taken before the completion of a large study of inflight exposures to ETS commissioned by the U.S. Department of Transportation (DOT) and without any evidentiary or other hearings. When the study was released several months later, it contained data indicating that individuals seated in nonsmoking sections are exposed to extremely low levels of ETS constituents.[17] In fact, many measured levels of ETS constituents were reported to be below the detection limits of the air sampling monitors. In a recent presentation, one of the principal scientists responsible for the study questioned "whether or not Congress knew that the ETS results were not strongly compelling prior to the study's release and as a result preempted the use of the results in the deliberations on whether or not to make the ban permanent."[18]

Research results and technical reviews available prior to the Congressional action also suggest that it was not based upon scientific data.[12,15,19-20] In 1988, a review of the relevant data concluded that "the available scientific evidence does not support the prohibition of smoking on commercial aircraft."[19] The review

2023469086

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

stated that the data "suggest that factors or substances other than ETS may be major contributors to subjective complaints of discomfort by passengers and flight crew." Similarly, in 1989, an Australian writer concluded that the available data "do not lend support to the hypothesis that exposure to environmental tobacco smoke may present a risk to the health of cabin staff or passengers."[20] He further observed that providing smoking and nonsmoking sections "meets the reasonable requirements of passengers."

One of the most comprehensive assessments of aircraft cabin air quality to date was undertaken in Europe in 1989.[12] The results indicate that total exposure to ETS aboard aircraft is "rather small and insignificant in comparison to total life exposure to air pollution." The researchers conducting the study concluded that any possible health effects from ETS exposures were "not likely to have been elicited" by exposures aboard flights. They also noted that reports of irritation and annoyance commonly attributed to ETS exposures may have been "potentiated by the low humidity, high temperature and high carbon dioxide levels found."

Governmental Reports

Governmental reports throughout the world, like the 1986 Report of the Surgeon General, have done little to clarify the

2023469087

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

scientific nature of the ETS issue for the public. In the United Kingdom, for instance, the Fourth Report of the Independent Scientific Committee on Smoking and Health (1988) endorsed the heavily criticized claim that ETS increases the nonsmoker's risk of lung cancer from 10 to 30 percent compared with the non-exposed nonsmoker,[21] although, as one commentator noted, "exposure data are very unreliable, and there is a proven basis for bias in the direction of exaggeration of the risk."[22] Still another U.S. governmental report concluded that exposure to ETS increases the risk of disease among nonsmokers, even though, when the authors sought to identify both the valid data and the areas of uncertainty regarding ETS, they observed "many more of the latter . . . than the former."[23] In addition, the most recent monograph on tobacco smoke from the World Health Organization's International Agency for Research on Cancer (IARC) warns of increased risks of disease among nonsmokers exposed to ETS while conceding that the epidemiological data are consistent "either with an increase or with an absence of risk."[24]

In June 1990, the U.S. Environmental Protection Agency (EPA) issued a public review draft risk assessment for ETS.[25] The review draft concluded that ETS is a cause of lung cancer in adult nonsmokers and respiratory disease in children, and that ETS is a Group A ("known human") carcinogen. The draft also estimated that ETS exposures are responsible for 3,800 lung cancer deaths a

2023469088

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

year among nonsmokers in that country. The draft was heavily criticized during the public review period by numerous scientists and researchers in the area, most notably because its authors failed to follow the EPA's own guidelines for risk assessment, in addition to addressing selectively the scientific literature and drawing conclusions which were not supported by the scientific data.[26] Despite the overwhelming scientific criticism, the Science Advisory Board, a review panel for the EPA, agreed with the conclusions in the draft and submitted its endorsement to the administrator of the agency. The director of the EPA will decide whether or not the draft will become part of the agency's policy.

In July 1991, the U.S. National Institute for Occupational Safety and Health (NIOSH) issued a "Current Intelligence Bulletin" on ETS in the workplace.[27] The Bulletin concludes that ETS is a potential occupational carcinogen and recommends that exposures be reduced "to the lowest feasible concentration." However, the Bulletin did not examine the data on actual workplace exposures to ETS or the information on workplace exposures to ETS which can be found in 11 studies on ETS exposures and lung cancer in nonsmokers. Those data provide no support for NIOSH's claims.

In June of 1991, the Environment Committee of Great Britain's House of Commons issued a report, entitled Indoor Pollution, which contained recommendations for government action

2023469089

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

on improving the indoor environment.[28] Prior to issuing its report, the committee heard presentations on ETS from individuals and organizations with widely varying views on the issue, including scientists with the British-American Tobacco Company (BAT) and representatives of the antismoking group Action on Smoking and Health (ASH). In its report, the committee acknowledged that there is a "scientific dispute" about the purported health effects of ETS, but urged that efforts be made to minimize nonsmoker exposure to ETS, and that children, in particular, should be "protected."

Still another recent governmental report on ETS, issued to the Minister and State Secretary for Welfare, Health and Cultural Affairs in the Netherlands, presented a critical assessment of the scientific literature on ETS.[29] While concluding that exposure to ETS increases the risk of disease in nonsmokers, the report also concluded, contrary to the U.S. EPA draft risk assessment, that the various "distorting factors" in reports on ETS preclude the possibility of making a well-founded estimate of the magnitude of so-called increased risk from ETS exposure.

Court Decisions

However, some governmental bodies have refused to give in to the emotional rhetoric of antismoking organizations and public health officials. For example, courts in the United States have,

2023469090

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

with few exceptions, denied the claims of individuals who contend they have a "right" to a smoke-free workplace. A law journal article noted that "the efforts of nonsmokers to restrict workplace smoking have met with little success in the courts, which have been reluctant to supplant the roles of employer and employee."[30]

Courts in other countries have also ruled on related issues. In 1987, the Supreme Court of Canada refused an appeal by a worker who sought a smoke-free environment on the grounds that ETS is a "dangerous" workplace substance.[31] Similarly, in Japan, a court judgment denied a plaintiff's request that more than half of all the railway cars on passenger trains be designated nonsmoking because, the Court ruled, ETS exposures do not "exceed the limits of normal tolerance."[32]

In another recent U.S. court case, an antismoking organization challenged the decision of the U.S. Occupational Safety and Health Administration (OSHA) not to issue an emergency temporary standard banning tobacco smoking in the workplace. An Appeals Court upheld the OSHA decision, stating that the agency "reasonably determined that it could not at this time sufficiently quantify the degree of risk associated with workplace exposure to ambient tobacco smoke to justify issuing an emergency temporary standard."[33]

2023469091

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

In 1990, the District Court of the Hague in the Netherlands ruled that the government-funded Dutch Foundation on Smoking and Health (StiVoRo) was not liable to the tobacco industry for its statement that ETS is "unhealthy" for nonsmokers. The Court recognized, however, that:

> In the present discussion over the consequences of passive smoking, the starting point must be that scientific investigation has not succeeded in establishing which facts are true and which are not true. It is evident from the documents that the discussion concerns a controversial subject, on which there are divergent - whether or not scientifically supported - opinions. From the documentary evidence it is likewise apparent that the results of medical research and positions taken within medical science with respect to the consequences of passive smoking also vary.[34]

In 1985, the Supreme Insurance Court of Sweden awarded compensation for occupational injury to the estate of a nonsmoker who worked with smokers and who subsequently died of lung cancer. Although the media described the Court's decision as a causal indictment of ETS exposure, one commentator noted that the decision was based upon the structure of occupational injury regulations in Sweden and not upon any scientific evidence of a causal relationship between lung cancer and ETS exposures.[35] This author explained that the Swedish insurance system operates under a reverse burden-of-proof provision, namely, that the relationship between a suspected factor and an injury is assumed to be causal unless

2023469092

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

substantially stronger reasons are produced to suggest otherwise. Consequently, this provision does not require the claimant to present scientific proof of a causal relationship between a suspected factor and an injury to be awarded compensation.

Three years later, in Australia, a city bus driver who contended his lung cancer was caused, at least in part, by exposure to ETS on the job made a claim against the Melbourne Transit Authority.[36] The matter was settled by the insurer of the Transit Authority. This settlement was interpreted by some as establishing a legal precedent for the claim that ETS exposure has been proven to cause lung cancer. However, the bus driver's claim regarding ETS was only part of his complaint, and the tribunal before which the proceeding was held heard only part of the evidence in the case before the insurer made a settlement offer.[37] Thus, this settlement established no formal legal precedent regarding ETS health claims.[36-37]

Several other recent court decisions have been heavily touted by antismoking organizations as important, precedent-setting cases regarding the adverse health effects from exposure to ETS. However, a careful examination of the context in which each of these cases was heard reveals the limited nature of the claims. For example, in April 1990, a social security commissioner in the U.K. ruled that an asthmatic employee of the social security

2023469093

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

administration had suffered specific adverse reactions after exposure to ETS.[38] However, the Commissioner's ruling pertained only to the question of whether or not an "accident" had occurred under the meaning of the 1975 Social Security Act.[39] The decision made no finding regarding the medical facts of the case, and no finding as to whether the claimant is disabled or whether any benefits will be granted. Indeed, the Commissioner noted that his decision establishes "no precedent for other cases" involving claimed ETS exposures. In addition, he noted that this was an "unusual case" with no application to the "ordinary case of alleged injury or disease" from exposure to ETS.[39]

Most recently, a court in Australia ruled in favor of the Australian Federation of Consumer Organizations (AFCO) in its allegation that a July 1986 advertisement on ETS by the Tobacco Institute of Australia (TIA) was false and "misleading and deceptive" under that country's Trade Practices Act. The case centered around the TIA's statement in the ad that "there is little evidence and nothing which proves scientifically that cigarette smoke causes disease in nonsmokers."[40] The Tobacco Institute of Australia has appealed the decision on the basis that their statement is "an opinion which has a rational scientific basis."[41]

2023469094

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Summary

Governmental involvement in the ETS question raises many disturbing questions. An Australian writer who recently addressed the issue cautioned that:

> Those involved in government anti-smoking activities should be aware of the tenuous nature of the data on passive smoking and health effects. The deliberate use of fear inducing tactics by misrepresenting such data by dubious extrapolations is propaganda and not health education.[42]

Similarly, a group of physicians in the U.S. observed that "scientific data have not always been utilized objectively by governmental agencies or regulatory bodies that have their own inherent public health or political agenda."[43] They concluded:

> The implementation of public policies must be based on good science, to the degree that it is available, and not on emotion or on political needs. Those who develop such policies must not stray from sound scientific investigations, based only on accepted scientific methodologies. Such has not always been the case with environmental tobacco smoke.

It is clear that once claims regarding environmental tobacco smoke and disease in nonsmokers are placed in their proper scientific perspective, the issue of prohibiting smoking in public places becomes a social and political one. The issue thus involves

2023469095

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

whether or not public policy should mandate the prohibition of smoking because it is seen by some as a nuisance or annoyance. If the decision is reached in favor of regulation, then one must decide whether the same line of reasoning applies to other kinds of "annoyances" encountered in everyday life and whether those "annoyances" should also be banned. The implication of such reasoning should be obvious to anyone who is opposed to unwarranted governmental intrusion into people's lives. As a German scientist recently concluded:

> Whether a real risk is involved which in the future can be demonstrated on the basis of measurable results remains an open question. In light of this health officials should concentrate on more significant environmental problems in the long term interest of society rather than wasting time and money on trivial issues.[44]

Conclusion

Smoking bans do not improve fresh air ventilation, nor do they ensure acceptable indoor air quality. Complaints about the quality of indoor air typically arise in poorly ventilated areas. For example, data from over a thousand "sick building" investigations in North America and Europe indicate that more than half of the buildings were inadequately ventilated, and that ETS was associated with occupant complaints in no more than four percent

2023469096

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

of all the cases. (For a discussion of this data, see the section on "Sick Building Syndrome.")

The importance of adequate ventilation for maintaining indoor air quality has been recognized by many researchers and organizations. The experience of the American Society of Heating, Refrigeration and Air Conditioning Engineers (ASHRAE), during its attempt to establish a ventilation standard which balances the need for adequate ventilation with the demand for little or no exposure to ETS, is instructive in this regard. Initially, the organization developed a standard which established ventilation rates solely on the basis of the presence or absence of smokers. However, the prescribed ventilation rates for nonsmoking areas were reported to be inadequate. Consequently, in 1989, the organization published a ventilation standard entitled "Ventilation for Acceptable Indoor Air Quality" (ASHRAE Standard 62-1989) which adopts a single ventilation rate with no distinction between smoking and nonsmoking areas.[45] According to knowledgeable researchers, the standard serves as a guide for preventing indoor air problems and for establishing ventilation rates for indoor areas in order to "control carbon dioxide and other contaminants with an adequate margin of safety, and to account for variations among people, varied activity levels, and a moderate amount of smoking."[46-48]

2023469097

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

An alternative to governmental regulation of smoking supports the notion of proper ventilation for all building occupants together with the promotion of courtesy and cooperation among smokers and nonsmokers. This solution is supported by data on indoor air quality and relies upon common sense, courtesy and the free marketplace for decisions concerning smoking. More importantly, however, this solution avoids unnecessary governmental interference with its subsequent loss of individual freedom.

2023469098

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

REFERENCES

ENVIRONMENTAL TOBACCO SMOKE AND THE PUBLIC

1. Larkin, D., "Executive Director's Report: The Emergence of the Nanny State," National (Australia) Business Bulletin, April, 1991.

2. Rylander, R., "Workshop Perspectives." In: ETS - Environmental Tobacco Smoke: Report from a Workshop on Effects and Exposure Levels. R. Rylander, Y. Peterson and M.-C. Snella (eds.). Published simultaneously in European Journal of Respiratory Diseases, Supplement 133, Vol. 65, 143-145, 1984.

3. Lehrer, S., et al., "Tobacco Smoke 'Sensitivity' -- Is There an Immunologic Basis?," J Allergy Clin Immunol 73(2): 240-245, 1984.

4. Winneke, G., et al., "Psychophysiological Response to Environmental Tobacco Smoke in an Experimental Setting." In: Indoor Air Quality. H. Kasuga (ed). Berlin, Heidelberg, Springer-Verlag, 173-183, 1990.

5. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health, The Health Consequences of Involuntary Smoking: A Report of the Surgeon General. DHHS Publication No. (CDC) 87-8398, Washington, D.C., U.S. Government Printing Office, 1986.

6. Fettner, A., "Where There's Smoke There's Ire -- The New 'Passive Smoking' Rules: Sidestepping Issues by Scapegoating Smokers," Voice, 5-7, March 30, 1987.

7. Jones, W., "Inconclusive Evidence on the Harmful Effects of Smoking," U.S. Congressional Record - Extensions of Remarks, E489-E490, February 18, 1987.

8. Vaughan, W. and Hammond, K., "Impact of 'Designated Smoking Area' Policy on Nicotine Vapor and Particle Concentrations in a Modern Office Building," J Air Waste Manage Assoc 40: 1012-1017, 1990.

9. Hedge, A., et al., "Building Ventilation and Smoking Policy Effects on Indoor Air Quality and Employee Comfort and Health." In: Indoor Air '90: Proceedings of the Fifth International Conference on Indoor Air Quality and Climate. Toronto, Canada, Volume 1, 739-744, July 29-August 3, 1990.

10. Sterling, T. and Mueller, B., "Concentrations of Nicotine, RSP, CO and CO_2 in Nonsmoking Areas of Offices Ventilated by

2023469099

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

Air Recirculated from Smoking Designated Areas," Am Ind Hyg Assoc J 49(9): 423-426, 1988.

11. Sterling, T., et al., "Exposure to Environmental tobacco Smoke in the Non Industrial Workplace Under Different Conditions of Ventilation and Smoking Regulation." In: Present and Future of Indoor Air Quality. C.J. Bieva, et al. (eds.). Elsevier Science Publishers, Amsterdam, 111-118, 1989.

12. Malmfors, T., et al., "Air Quality in Passenger Cabins of DC-9 and MD-80 Aircraft," Environ Technol Letters 10: 613-628, 1989.

13. Oldaker, G., et al., "Estimation of Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft II." In: Indoor Air Quality and Ventilation, F. Lunau and G. Reynolds (eds.). London, Selper Ltd., 447-454, 1990.

14. Sterling, T. and Mueller, B., "Concentrations of Nicotine, RSP, CO and CO_2 in Nonsmoking Areas of Offices Ventilated by Air Recirculated from Smoking Designated Areas," Am Ind Hyg Assoc J 49(9): 423-426, 1988.

15. Oldaker, G. and Conrad, F., "Estimation of the Effect of Environmental Tobacco Smoke on Air Quality Within Passenger Cabins of Commercial Aircraft," Environ Sci Technol 21: 994-999, 1987.

16. Sterling, T., "ETS Concentrations Under Different Conditions of Ventilation and Smoking Regulation." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 89-98, 1988.

17. Nagda, N.L., et al., GEOMET Technologies, Inc., "Airliner Cabin Environment: Contaminant Measurements, Health Risks, and Mitigation Options: Final Report," U.S. Department of Transportation, Report No. DOT-P-15-89-5, December 15, 1989.

18. Baker, S., "Health Risks to Airliner Occupants: Exposures to Environmental Tobacco Smoke and Other Pollutants," Presentation, ILSI Risk Science Institute, Brookings Institution, Society for Risk Analysis, June 14, 1990. Transcript.

19. Holcomb, L., "Impact of Environmental Tobacco Smoke on Airline Cabin Air Quality," Environ Technol Letters 9: 509-514, 1988.

20. Crawford, W., "Environmental Tobacco Smoke in Airliners--Health Issues," Aerospace: 12-17, July, 1989.

2023469100

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

21. Department of Health and Social Security, Fourth Report of the Independent Scientific Committee on Smoking and Health, London, Her Majesty's Stationery Office, 1988.

22. Roe, F., "Passive Smoking," Lancet I: 888, April 16, 1988.

23. Committee on Passive Smoking, Board of Environmental Studies and Toxicology, National Research Council, National Academy of Sciences, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects. Washington, D.C., National Academy Press, 1986.

24. World Health Organization, International Agency for Research on Cancer, IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Tobacco Smoking, Volume 38, Lyon, 1985.

25. U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Office of Atmospheric and Indoor Air Programs, Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children, External Review Draft, EPA 600/6-90/006A, May, 1990.

26. Anonymous, "A Brief Summary of the Public Comments Submitted to the U.S. EPA in Response to the External Review Draft EPA/600/6-90/006A," Submitted to the U.S. Environmental Protection Agency, Science Advisory Board Meeting, 1-20, December 4-5, 1990.

27. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, Current Intelligence Bulletin 54: Environmental Tobacco Smoke in the Workplace: Lung Cancer and Other Health Effects. DHHS (NIOSH) Publication No. 91-108, Cincinnati, Ohio, June, 1991.

28. House of Commons Environment Committee, United Kingdom, Indoor Pollution. London, Her Majesty's Stationery Office, June 12, 1991.

29. Health Council Committee on Passive Smoking, "Passive Smoking: Assessment of the Harmfulness to Health of Environmental Tobacco Smoke: Report of the Health Council Committee on Passive Smoking to the Minister and State Secretary for Welfare, Health and Cultural Affairs," The Hague, Netherlands, No. 1990/18, December 10, 1990. Translation.

30. D. Vaughn, "Smoking in the Workplace: A Management Perspective," Emp Rel Law J 14(3): 359-386, Winter, 1988.

2023469101

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

31. Anonymous, "Court Upholds Appeal Ruling on ETS," Tobacco Reporter 114(6): 12, June, 1987.

32. "Summary of Court Judgment Relating to Rights for Anti-Smoking," District Court, Tokyo, Japan, Ruling, 1987. Translation.

33. Judgment, Action on Smoking and Health v. Occupational Safety and Health Administration, United States Court of Appeals for the District of Columbia Circuit, No. 89-1656, September Term, 1990.

34. Judgment, Stichting Sigaretten Industrie v. Stichting Volksgenzondheid En Roken, The Hague, October 31, 1990. Translation.

35. Zethraeus, S., "Arbetsskade - forsakringen ar formanlig men domen bevisor inte att passiv rokning ger cancer (Occupational Injury Insurance is Beneficial but the Judgment Does Not Prove that Passive Smoking Leads to Cancer)," Lag Avtal 1: 31-32, 1986. Translation.

36. Chan, G. and Mcdonnell, D., "No Jobs If You Smoke: Bosses," The (Sydney, Australia) Daily Telegraph, July 22, 1988.

37. Tobacco Institute of Australia, Press Release, "Sean Carroll Settlement," July 21, 1988.

38. O'Sullivan, J., "Asthma Sufferer Wins Case Over Passive Smoking Claims," The (London) Independent, August 30, 1990.

39. Goodman, M.J., Social Security Commissioner, Decision re: Joan Clay, Social Security Acts 1975 to 1986, Case No:2:11:1935, July 16, 1990.

40. Morling, J., Order Re Australian Federation of Consumer Organizations Inc. v. The Tobacco Institute of Australia Limited, Federal Court of Australia, New South Wales District Registry, General Division, No. G. 253 of 1987, February 7, 1991.

41. Tobacco Institute of Australia, Press Statement, "Tobacco Institute of Australia Limited ATS Australian Federation of Consumer Organizations Inc.," February 7, 1991.

42. Crawford, W., "Health Effects of Passive Smoking in the Workplace." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 203-210, 1988.

2023469102

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000

43. Huber, G., et al., "Passive Smoking: How Great a Hazard?," Consumers Research 74(7): 10-34, July, 1991.

44. Adlkofer, F., "Biological Effects After Exposure to ETS." In: Indoor Air Quality: Symposium. Buenos Aires, National Academy of Sciences of Buenos Aires, 61-76, 1989.

45. American Society of Heating, Refrigerating and Air-Conditioning Engineers, "ASHRAE Standard 62-1989, Ventilation for Acceptable Indoor Air Quality," Atlanta, ASHRAE Publications, 1989.

46. Goodfellow, H. and J. Wyatt, "Critical Review of Ventilation Contaminants in Indoor Air." In: Indoor Air Quality and Ventilation. F. Lunau and G. Reynolds (eds.). London, Selper Ltd., 95-104, 1990.

47. Binnie, P., "The Role of Ventilation in Controlling the Quality of Indoor Air, Including ETS." In: Other Peoples's Tobacco Smoke. A. Armitage (ed). Beverly, East York, United Kingdom, Galen Press, 159-172, 1991.

48. Burroughs, H., "ASHRAE: Addressing the Indoor Air Quality Challenge With Energy Conscious Design." In: Indoor and Ambient Air Quality. R. Perry and P. Kirk (eds.). London, Selper Ltd., 530-535, 1988.

2023469103

Source: https://www.industrydocuments.ucsf.edu/docs/tyxj0000